A.M.A.

Archives OF SURGERY

NOVEMBER 1955 VOLUME 71 NUMBER 5

HONOR AWARD FOR DISTINGUISHED SERVICE IN MEDICAL JOURNALISM

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RUPTURE OF ILIAC ANEURYSM INTO DUODENUM — PAUL D. ABRAMSON, M.D., ET AL.

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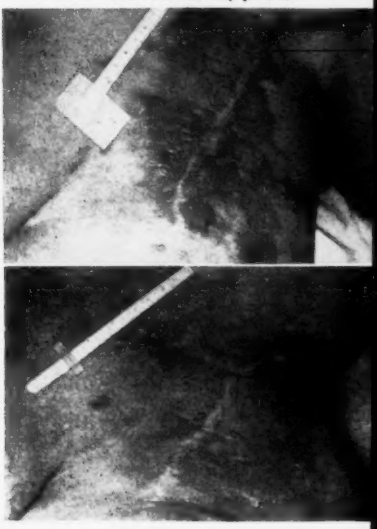

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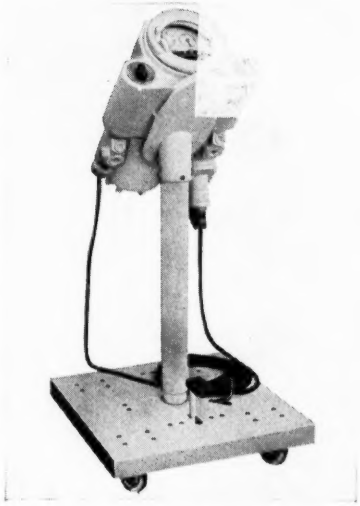

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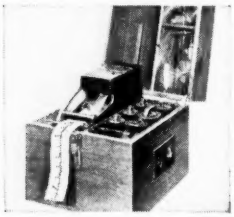

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For Distinguished Service in Medical Journalism

The A. M. A. ARCHIVES OF SURGERY, of which Dr. Waltman Walters has been the Chief Editor since 1940, has been selected as the recipient of the Honor Award of the American Medical Writers' Association for Distinguished Service in Medical Journalism in 1955. This is presented to the journal with a subscription of over 3000 which is devoted to some specialty in medicine or medical science "for accuracy, clarity and conciseness of published articles, editorials and other material, and/or distinguished and meritorious service rendered by a United States or Canadian medical periodical."

The committee for review of the Journals for the award is composed of Morris Fishbein, M.D., Chicago, formerly Editor, *Journal of the American Medical Association*, Chairman; Richard M. Hewitt, M.D., Rochester, Minn., Assistant Professor of Medical Literature, Mayo Foundation, and Dean F. Smiley, M.D., Chicago, Editor, *Journal of Medical Education*.

Dr. Waltman Walters, as Chief Editor, accepted the award on behalf of the A. M. A. Archives of Surgery at the meeting of the American Medical Writers' Association in St. Louis, on Friday, Sept. 30.

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A.M.A. Archives OF SURGERY

Bilateral Adrenalectomy in the Treatment of Cancer of the Breast

THOMAS L-Y. DAO, M.D.
and
CHARLES HUGGINS, M.D., Chicago

The treatment of mammary cancer by endocrine methods rests on the concept of hormonal dependence, which characterizes many of these neoplasms. It has been shown that some methods of alterations in endocrine balance can constitute effective palliation in many cases. Surgical castration and administration of sex steroids have been used as the chief therapeutic armamentarium for metastatic cancer of the breast in the past decade and a half. In 1951 an important method of treatment of the disease was introduced by the finding that in certain types of mammary cancer there is an adrenal component which sustains and propagates the disease.[1] Surgical excision of the adrenal glands in patients maintained on cortisone has proved to be effective in producing regression of mammary cancer in certain cases.*

Submitted for publication June 23, 1955.

From the Ben May Laboratory for Cancer Research of the University of Chicago.

This study was aided by grants from the Jane Coffin Childs Memorial Fund for Cancer Research, from the American Cancer Society on recommendation of the Committee on Growth of the National Research Council, and from the Illinois Division of the American Cancer Society. Cortisone was provided by Merck & Co., Inc., Rahway, N. J.

* References 2 and 3.

In his Hunterian lecture Cade[11] commented, "Bilateral adrenalectomy is an encouragement in the pursuit of an ideal which is to control cancer by an attack in the medium in which it grows as well as in a direct attack on the cancer." We agree with Cade,[12] who said, "In a proportion of cases both subjective and objective improvement has been achieved which has never been accomplished before by any other method of treatment."

Beatson showed, in 1896, that regression of mammary cancer could occur after the excision of ovaries. Though this work was done before there was any concept of endocrinology, it nevertheless showed that ovaries could be a factor in sustaining carcinoma of the breast. It is now known that the ovarian hormones, specifically the estrogenic compounds, are important causative factors of mammary cancer in mice.[4] It has also been observed that after the removal of the gonads compensatory hypertrophy and increased function of the adrenal cortex can occur. In certain stocks of mice gonadectomy induces adrenal hypertrophy, with, later, the formation of adrenal cortex tumors and frequently the development of cancer of the breast.[5] In recent years in our laboratory we have found that women with cancer of the breast who have undergone oophorectomy often continue to excrete significant and even large amounts of estrogenic compounds in the urine.[6] From this evidence it is clear that both the adrenal cortex and

the ovary are capable of secreting hormones that can sustain the growth of mammary cancer. These considerations led to the application of bilateral adrenalectomy and oophorectomy for human breast cancer.

PREOPERATIVE AND POSTOPERATIVE CARE OF THE PATIENT FOR TOTAL BILATERAL ADRENALECTOMY

The patient with advanced metastatic breast cancer who is to undergo adrenalectomy is frequently in poor state of nutrition, and it may be necessary to correct the lowered blood volume and the plasma proteins by repeated blood transfusions before operation. A careful evaluation is made of the renal, pulmonary, and cardiac status of the patient, for it is in these systems that the most serious postoperative complications are seen.

In surgery of the adrenal glands, adrenal insufficiency must be forestalled, as first brought out by Walters and Kepler [7]; it is difficult to correct postoperatively. It is a safe rule in any proposed extirpation of the adrenal to treat the patient in advance as if adrenal insufficiency were certain to develop postoperatively and to lessen the dosage of the essential hormones slowly in the days after the operation.

The hormonal substitution therapy essentially involves the use of rather large amounts of cortisone acetate the day preceding the operation and the operation day. On subsequent days the amount of cortisone is gradually reduced. The amount of desoxycorticosterone acetate (Doca) given will depend on how rapidly the blood pressure becomes stabilized at a satisfactory level. Frequently by the sixth postoperative day the patient will be on the future maintenance oral dose of cortisone acetate and sodium chloride.[8]

Fluids given during and immediately after the operation must be maintained at a moderate amount to avoid excessive hydration. Usually 500 ml. of plasma or blood is adequate during the operation, unless significant hemorrhage is encountered. Following the operation, 500 ml. of 5% dextrose in isotonic saline solution and 1000 to 1500 ml. of 5% dextrose in water are given slowly over the next 12 to 18 hours. Fluids by mouth are given as soon as tolerated. Excessive hydration of patients receiving large amounts of desoxycorticosterone acetate and cortisone may precipitate fatal pulmonary edema.

Severe hypotension at shock level can frequently be corrected by use of a vasopressor substance such as arterenol (Nor-epinephrine) in a concentration of 10γ per milliliter of saline solution and given intravenously at a rate which will give adequate blood-pressure levels. This has been rarely necessary in our experience. If hypotension is the result of hemorrhage, blood transfusion of course should be used. Shock as a result of sudden removal of adrenal glands does not occur if the patient is adequately prepared preoperatively. However, in a few instances, especially in those who had large adrenal glands, hypotension developed postoperatively. In these cases the lowered blood pressure was easily corrected by the use of hydrocortisone intravenously in a dose of 100 mg. given within a period of four hours. Rapid infusion of hydrocortisone is of no effect, since it will be excreted rapidly.

HORMONAL MAINTENANCE OF THE ADRENAL-LESS PATIENT

Criterion for the adequate hormonal substitution of the adrenalectomized patient was the prevention of any sign or symptom of adrenal insufficiency. Probably the best indicator has been the sense of well-being of the patient. The patient becomes quickly aware of a sense of malaise, and anorexia, and loss of the sense of well-being when on an inadequate dose of cortisone. These symptoms are frequently seen before any changes in blood pressure, blood sugar, or blood electrolytes are observed. They are usually quickly corrected by a small increase in cortisone dosage. We attempt to maintain the patient in normal electrolyte and carbohydrate balance and with adequate blood pressure without orthostatic hypotension. We have used cortisone acetate orally in doses of 37.5

and 50 mg. daily; it seems unwise to use dosages less than 37.5 mg. daily. Patients are given added sodium chloride in dose levels of 1 to 3 gm. a day. When maintained adequately, adrenalectomized patients have a healthy appearance, are not incapacitated, and are able to engage in most of their usual activities. Desoxycorticosterone acetate has been used in patients with orthostatic hypotension and has been given to patients whom we believed are adequately maintained on cortisone, without any increase in the sense of well-being or increased ability to do work.

CLINICAL INVESTIGATION

All of the patients had far-advanced mammary cancer, and all had distant metastases. The cases were unselected except for all having extensive disease, and they were consecutive. All, except two women, had been subjected to unilateral or bilateral mastectomy previously. Each case was verified by microscopic examination of the tissue.

A total of 175 patients with metastatic cancer of the breast were treated by adrenalectomy, 2 men and 173 women, since 1951 in this clinic (as of May, 1955). The initial mortality (death within 30 days of the operation) was 5% (in the first 100 cases). There has been one postoperative death in the last 75 cases. The first 100 consecutive cases operated on in this clinic during the three-year period 1951-1953 are valid for evaluation. There were 5 deaths out of these 100 cases. Among the 95 effective cases 34 cases had adrenalectomy alone and 61 cases had a combined procedure of adrenalectomy and oophorectomy done. Objective remissions of varying duration have occurred in 14 of the 34 patients who had adrenalectomy alone (41%) and in 25 of the 61 cases (41%) with a combined procedure of adrenalectomy and oophorectomy (Table 1 and 2). Assessment was based on both objective and subjective evidence of improvement. Objective improvement is often profound; it is measured by regression or disappearance of obvious and easily accessible lesions, such as cutaneous and subcutaneous tumors and intra-abdominal masses, and also by x-ray evidence of calcification of osteolytic lesions and healing of fractures and of disappearance of pulmonary lesions and pleural fluid. Subjective improvement is often remarkable, especially in the relief of bone pain, disappearance of respiratory symptoms, and presence of a sense of well-being. Subjective and objective improvements are not always concomitant. In many patients who show marked subjective improvement

TABLE 1.—*Bilateral Adrenalectomy for Metastatic Breast Cancer*

Total Cases, No.	34
Cases with Objective Response, No.	14 (41%)

Alive (6 Cases)		Dead (8 Cases)	
Survival, Mo.	Cases, No.	Survival, Mo.	Cases, No.
18	1	9-12	7
29-38	3	24	1
44-48	2	.....	..

TABLE 2.—*Bilateral Adrenalectomy and Oophorectomy for Metastatic Cancer of the Breast*

Total Cases, No.	61
Cases with Objective Response, No.	25 (41%)

Alive (14 Cases)		Dead (11 Cases)	
Survival, Mo.	Cases, No.	Survival, Mo.	Cases, No.
18-22	9	8-10	2
25-29	3	12-13	7
38-41	2	24	2

there is no demonstrable improvement in the lesions. Remission of disease following adrenalectomy therefore is assessed by objective evidence of improvement, and subjective improvement alone is not counted. Profound regression of the cancer has persisted from two and one-half years to four years in eight patients after the operation. A brief survey of six cases follows.

REPORT OF CASES

CASE 1.—This was the first patient with mammary cancer treated by bilateral adrenalectomy and has some historical interest on this account.

A woman, aged 46, first discovered a lump in her left breast in July, 1949. Radical mastectomy was

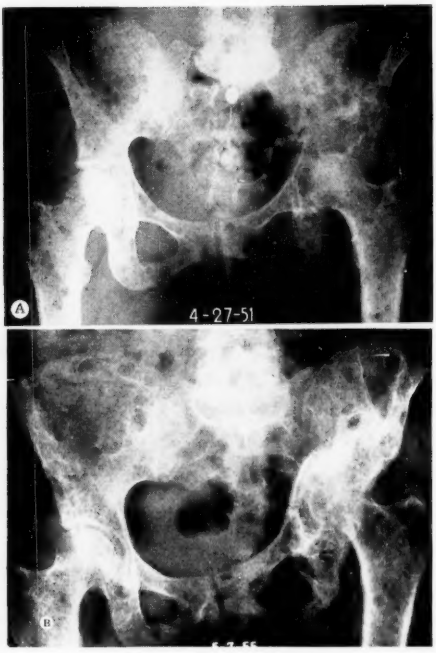


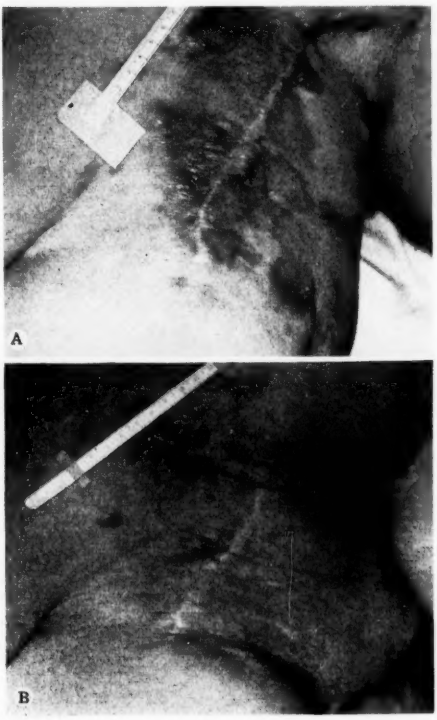
Fig. 1 (Case 1).—*A*, extensive osteolytic metastatic lesions with multiple pathological fractures in pelvis, secondary to mammary cancer, before adrenalectomy. *B*, healing of pathological fractures and recalcification of osteolytic lesions four years after adrenalectomy.

done on Dec. 9, 1949. Postoperative radiation therapy was given. Osseous metastases became evident in January, 1951, and she was treated with testosterone, with no relief. Rapid progression of osseous metastases followed, and the patient became confined to bed in February, 1951, with multiple fractures of the pubis, ischium, and pelvis. Ethinyl estradiol was given after testosterone failed to produce any relief. This too showed no effect. Hypercalcemia developed while the patient was bedridden with extensive osseous lesions. There had been a left oophorectomy done in 1930 for ectopic pregnancy. Menstruation ceased after irradiation of pelvis in February, 1951. Bilateral adrenalectomy was performed on May 7, 1951. There has been steady improvement since the operation, with healing of fractures (Fig. 1). The patient is free from pain and is ambulatory and able to do all housework. Four years have elapsed since the operation.

Case 2.—A woman, aged 61, was treated by radical mastectomy in 1949. When she was first seen in this clinic, in August, 1951, there was an extensive local recurrent inflammatory carcinoma over the left chest wall and a large tumor in the contralateral breast, with nipple retraction. Breast biopsy proved the tumor to be cancer. Adrenalectomy was done on Sept. 5, 1951. The local recurrent lesion rapidly regressed within a month after operation (Fig. 2). The retraction of the nipple of the right breast disappeared, and the mass became nonpalpable. The patient has remained well for 44 months.

Case 3.—A woman, aged 41, first discovered a lump in the right breast in 1942. It was treated by a simple mastectomy with postoperative radiation in the following month. Local recurrence in the mastectomy scar in 1946 was treated by x-ray and by surgical excision in 1948. In August, 1951, she developed severe left chest pain with cough, dyspnea, orthopnea, and marked edema of the right arm. X-ray confirmed the presence of hydropneumothorax in the left chest. Repeated thoracentesis was done at weekly intervals to relieve the symptoms. The patient became bedridden. Testosterone, 50 mg., was given three times a week for two months, with no improvement. Menopause was induced by testosterone in September, 1951. Bilateral

Fig. 2.—*A*, extensive local recurrent inflammatory lesion over the mastectomy scar before adrenalectomy. *B*, regression of skin lesion 32 months after operation.



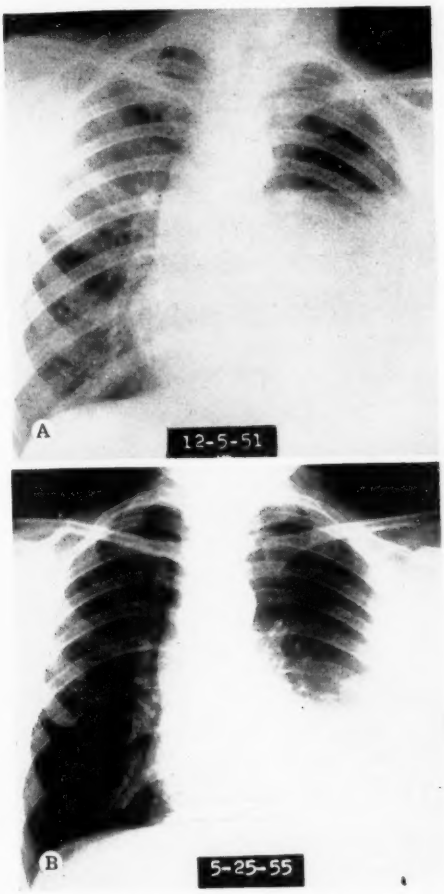


Fig. 3 (Case 3).—*A*, hydropneumothorax of the left pleural cavity before adrenalectomy. *B*, resorption of pleural effusion 42 months after operation.

oophorectomy and adrenalectomy were performed on Dec. 19, 1951. There was almost immediate relief of the respiratory symptoms and resorption of the pleural fluid (Fig. 3). Thoracentesis has not been required since the operation. Edema of the arm has desappeared. The patient is in excellent health 42 months after the operation.

Case 4.—A woman, aged 58, discovered a lump in her left breast in February, 1949. Radical mastectomy was done in March, 1949. Postoperative radiation was given. Spontaneous menopause occurred in 1944, when the patient was 50. In December, 1951, the patient developed osteolytic metastases in the pelvis and spine, accompanied by severe pain. She became bedridden in February, 1952, after a compression fracture of L-3. The patient was given testosterone in large doses in February and March, with no relief of pain. A pathological fracture of the left femur occurred in March, 1952. Bilateral adrenalectomy was performed on March 22, 1952, and bilateral oophorectomy, in October, 1952. There has been filling in of the osseous lesion, healing of pathological fracture, and disappearance of bone pain, and the patient has been ambulatory for more than three years after adrenalectomy.

Case 5.—A man, aged 51, was treated by radical mastectomy in 1946. This was followed by radiation to chest wall, axilla, and supraclavicular region. A pleural effusion appeared in June, 1948, but this subsided in August, 1948, following orchiectomy. In December, 1951, he noticed pleuritic pain in the left chest, with pleural effusion. Thoracentesis was performed twice. On each occasion the fluid was bloody and cytological studies were positive for cancer. Adrenalectomy was performed on April 19, 1952, and this was followed by disappearance of pleural fluid. No thoracentesis has been required since, and the patient has been in excellent health for more than three years.

Case 6.—A woman, aged 48, first noticed a lump in her right breast in March, 1951. Radical mastectomy was done in March, 1951, followed by local x-ray irradiation. In July, 1952, the patient noticed pain in her left chest accompanied by exertional dyspnea. X-ray confirmed the presence of large pleural effusion in the left chest. Repeated thoracentesis was done in weekly intervals, with temporary relief of respiratory symptoms. Pleural fluid was positive in cytology examination. In September, 1952, Au^{189} was given intrapleurally. Thoracentesis was done three times afterward, with an interval of about one month each. The patient developed a cough. Testosterone propionate was given three times a week for two months, with no improvement. Menopause was induced at the age of 44, after the radium treatment for menorrhagia, in 1948. On Jan. 30, 1953, bilateral adrenalectomy and oophorectomy were performed. The ovaries were sclerotic and atrophic. Immediate relief of respiratory symptoms was observed after the operation. There was resorption of fluid, and thoracentesis has not been required after adrenalectomy. The patient is in excellent health two and one-half years after the operation.

ALKALINE PHOSPHATASE IN SERUM AND URINARY CALCIUM IN CASES OF MAMMARY CANCER BEFORE AND AFTER ADRENALECTOMY

Since osseous metastases are common in cancer of the breast, alkaline phosphatase and urinary calcium determinations are use-

TABLE 3.—*Alkaline Phosphatase in Cases of Mammary Cancer with Osseous Metastases Before Adrenalectomy*

Range *	Cases, No.
6.1-10	18
10.1-20	23
20.1-30	8
30.1-40	5
40.1 and up	4†

* King-Armstrong units/100 cc. of serum.
† Three with extensive osteoblastic changes of the bone after extensive testosterone therapy and one with extensive osteolytic metastases.

ful in studying the course of the disease, especially in assessing whether therapy has been effective. The elevations in serum alkaline phosphatase indicate an increased osteoblastic activity or disease of the liver. In women who have advanced cancer of the breast with osteolytic metastases, elevation of alkaline phosphatase in serum after therapy and its subsequent decline to normal values is regarded as indicating increase of osteoblastic activity of bone and healing of metastases. In this laboratory 10 King-Armstrong units in 100 cc. of serum is regarded as the upper limit for normal adults. The preoperative values of alkaline phosphatase in 58 women with moderate to extensive osseous metastases from breast cancer are shown Table 3. In patients with icteric serum, high values of alkaline phosphatase were attributed to involvement of the liver and were not included. (These cases were subsequently confirmed to have liver metastases at the time of the operation.) Of 24 cases with response following adrenalectomy, the alkaline phosphatase rose to levels higher than the preoperative levels in 20 cases. Accompanying the change of the level of this enzyme, there was x-ray evidence of healing of pathological fractures and of calcification of osteolytic lesions.

Urinary calcium studies in patients with metastatic breast cancer provide a sensitive and objective measure of the rate of tumor growth. It rests on the presence of osteolytic activity of bones. Urinary calcium studies are of no value in patients without (or with minimal) bone metastases. Hyperparathyroidism and osteoporosis are also causes of hypercalcuria and hypercalcemia, but they can easily be differentiated by clinical and laboratory tests.

The presence of hypercalcuria and hypercalcemia in advanced mammary cancer indicates rapid bone destruction due to the metastatic disease. The serum calcium, however, does not rise above normal until the

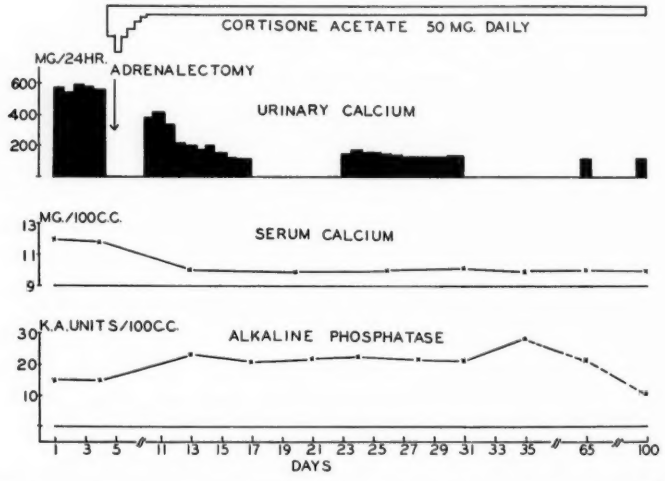


Fig. 4.—Changes in urinary calcium excretion, serum calcium, and serum alkaline phosphatase following adrenalectomy in a woman with metastatic cancer of the breast. There was marked regression of skeletal metastases after the operation.

urinary calcium excretion reaches a very high level, usually above 500 mg. per day. The urinary calcium excretion levels in eight cases with minimal of osseous lesions were determined, and they were all within the normal limits. In patients with a moderate amount of osseous metastases the urinary calcium excretion level is elevated. The level of the excretion often is parallel to the extension of the bone involvement. But this is by no means always true. We have observed normal urinary calcium excretion levels in patients with a considerable amount of bone metastases. It has also been observed that the lowering of the urinary calcium excretion level after therapy does not necessarily mean that there is cessation of bone destruction. Four patients whose urinary calcium excretion decreased to normal levels after cortisone therapy showed progression of bone lesions on roentgenologic examination. In most cases, however, it is observed that when remission occurs after effective therapy in cancer of the breast the high level of urinary calcium usually declines to normal. Symptoms of hypercalcemia disappear within a short period of time (Fig. 4). In this laboratory the range of urinary calcium in normal persons is 60 to 140 mg. for 24 hours.

CHARACTERISTICS OF ADRENAL-DEPENDENT MAMMARY CANCER

Histologic Specificity.—It is now evident that not all mammary cancer is responsive to the removal of adrenal glands. Only certain types are adrenal-dependent. The recognition of such type of tumor is of utmost importance for better selection of cases for adrenalectomy. We have found that the microscopic appearance of the primary or the metastatic lesions of the breast is of value in determining prognosis. The most responsive tumors are composed of spheroids of microscopic size in which the malignant acini have lumina whose lining is one cell in thickness. The tiny globules contain a secretion which maintains the acini in spheroidal forms. Often the metastatic lesions of this type of tumor maintain the original histology of the primary lesion, i. e., with the formation of glands. We regard this type of tumor (glandular adenocarcinoma) as a specific functional category of mammary cancer. This type is often hormone-dependent.

It is evident that it is impossible to deduce the function of cells with precision from the morphologic appearance of a tumor. The fact that mammary carcinomas seldom are monomorphous in cytology inhibits any accurate correlation of the morphology to the response to adrenalectomy. It was, however, observed in our study that when well-differentiated adenocarcinoma was present predominantly, although associated with some other types of tumors, regression generally followed adrenalectomy (Fig. 5). In 38 cases with a favorable response to adrenalectomy 28 cases (73%) had adenocarcinoma, 6 cases had duct carcinoma, and 4 cases had papillary carcinoma. In none of these cases was a single tumor present; they were all mixed tumors. Classification of these tumors therefore depends on the presence of a particular type of tumor in predominance. It was also shown in these 38 responsive cases that response to adrenalectomy could occur in cancers other than adenocarcinoma. It is necessary to point out that only women with adenocarcinoma of the breast enjoy profound and prolonged regression. All six patients who are living from three to four years since adrenalectomy had adenocarcinoma. Only one patient among six with duct carcinoma had remission of two years after bilateral adrenalectomy. We have not yet observed any regression in patients with undifferentiated mammary carcinoma.

Hormonal Excretion.—Since it was found in this laboratory that women with cancer of the breast who have undergone oophorectomy or ovarian irradiation continue to excrete estrogenic hormones in the urine, a comparison of the level of excretion between responsive and nonresponsive cases was made. The excretion of estrogen in 40 women with cancer of the breast in these two groups was appreciably different. The excretion level of 20 unresponsive cases

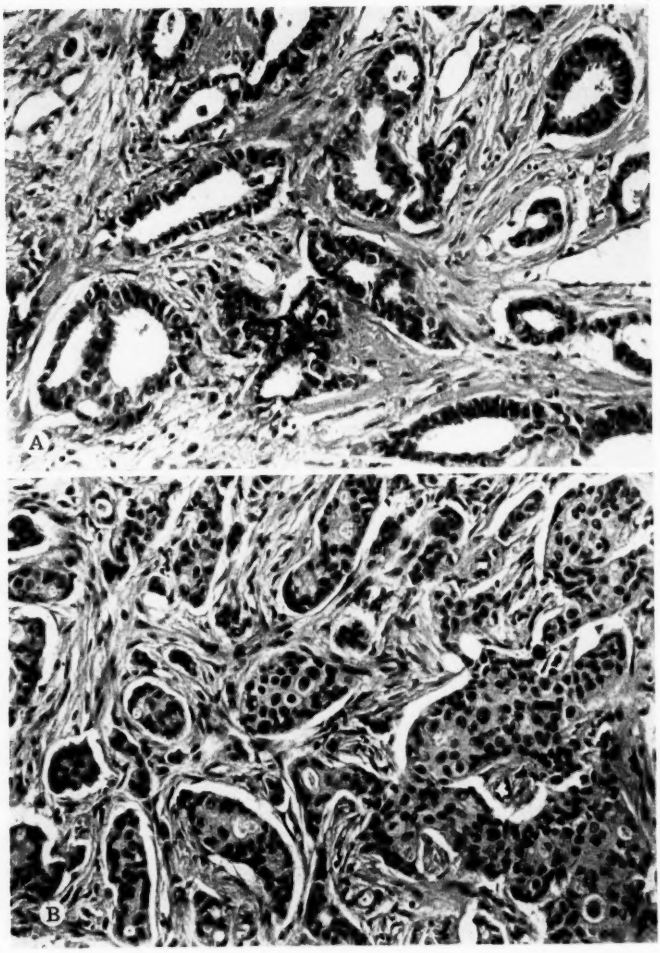


Fig. 5 (Case 4).—Photomicrographs of two different fields from the same microscopic section of the primary breast carcinoma in a patient who had marked regression of skeletal metastases after adrenalectomy; reduced from Mag. × 325.

ranged from 3.7 to 16.8 I. U. per 24 hours, with median and mean values of 8.4 I. U. per 24 hours (Table 4), whereas that of responsive cases was 10.6 to 58.9 I. U. per 24 hours, with an average of 22.1 I. U. and median value of 16.5 I. U. per 24 hours (Table 5). This is approximately a threefold difference between these two groups of cases. This observation indicates that women with high estrogen titer in urine respond better to adrenalectomy than those who excrete small amounts of estrogen substances.

THE USE OF ANDROGENS, ESTROGENS, AND CORTISONE IN PATIENTS WITH RELAPSE FOLLOWING ADRENALECTOMY

Both androgens and estrogens have been used in patients who either fail to respond to adrenalectomy or have relapse after a period of remission following the operation. Testosterone therapy was used in 12 patients who had adrenalectomy previously. Among these patients five had previously responded to adrenalectomy and seven had

TABLE 4.—*Estrogen Excretion in Urine in Women with Cancer of Breast Unresponsive to Adrenalectomy*

Patients	Age, Yr.	Cause of Menopause	Estrogen Titer in Urine, I. U./24 Hr.*	Histology
M. Q.	57	Surgical	9.6	Undifferentiated
L. P.	45	Irradiation	4.7	Undifferentiated
V. C.	47	Irradiation	12.3	Duct carcinoma
M. S.	36	Irradiation	3.7	Duct carcinoma
K. A.	49	Irradiation	9.2	Poorly differentiated adenocarcinoma
M. S.	50	Irradiation	6.7	Undifferentiated
V. R.†	47	Surgical	16.0	Adenocarcinoma
E. Z.†	31	Surgical	8.4	Undifferentiated
L. W.†	60	Spontaneous (6 yr.)	8.8	Poorly differentiated adenocarcinoma
L. B.†	49	Spontaneous (3 yr.)	3.7	Papillary carcinoma
G. S.	50	Surgical	12.0	Undifferentiated
A. S.	57	Spontaneous (6 yr.)	9.0	Undifferentiated
M. E.	40	Irradiation	8.2	Undifferentiated
I. P.	47	Surgical castration	7.5	Undifferentiated
F. M.†	69	Postmenopausal (22 yr.)	10.0	.....
C. K.	33	Surgical	5.0	Undifferentiated
M. K.	53	Surgical	5.3	Undifferentiated
L. P.	57	Irradiation	5.0	Adenocarcinoma
S. P.	63	Postmenopausal (6 yr.)	15.5	.....
J. D.	29	Surgical	8.4	Undifferentiated

* One international unit is equivalent to 0.1γ of estrone.
† Subjective improvement occurred in these cases.

TABLE 5.—*Estrogen Excretion in Urine in Women with Cancer of Breast Responsive to Adrenalectomy*

Patients	Age, Yr.	Cause of Menopause	Estrogen Titer in Urine, I. U./24 Hr.*	Histology
M. W.	45	Surgical	38.0	Adenocarcinoma
C. K.	60	Spontaneous (8 yr.)	16.0	Adenocarcinoma
A. M.	52	Spontaneous (3 yr.)	15.0	Duct carcinoma
M. A.	52	Irradiation	58.9	Adenocarcinoma
A. M	32	Surgical	18.6	Adenocarcinoma and duct carcinoma
A. B.	49	Spontaneous (3 yr.)	11.7	Adenocarcinoma
Y. S.	59	Surgical	22.0	Adenocarcinoma
N. D.	65	Surgical	12.5	Papillary adenocarcinoma
B. G.	42	Irradiation	28.2	Adenocarcinoma
I. J.	54	Spontaneous (6 yr.)	16.0	Adenocarcinoma
M. L.	34	Irradiation	39.8	.....
F. M.	55	Postmenopausal (5 yr.)	40.2	Duct carcinoma
A. Me.	51	Postmenopausal (4 yr.)	11.5	Adenocarcinoma
D. L.	57	Surgical	16.5	.....
R. B.	54	Irradiation	12.8	Poorly differentiated adenocarcinoma
R. G.	61	Postmenopausal (9 yr.)	21.0	Adenocarcinoma
M. S.	68	Postmenopausal (17 yr.)	16.2	Adenocarcinoma
E. L.	64	Postmenopausal (11 yr.)	21.0	.....
D. W.	28	Irradiation	10.6	Papillary adenocarcinoma
N. K.	68	Postmenopausal (21 yr.)	15.2	Adenocarcinoma
		Median 16.5 yr.	Mean 22.1	

* One international unit is equivalent to 0.1γ of estrone.

failed to demonstrate any beneficial effects from the operation. The duration of testosterone administration varied from three weeks to six months. In none of the cases was an objective remission observed.

Since it was believed that patients who failed to show initial response to the excision of ovaries and adrenal glands had estrogen-independent cancer, estrogenic compounds were given to seven patients of this category.

Diethylstilbestrol, 17-β-estradiol, and estriol were used. No objective remission was observed in any of these patients. In two instances the disease was definitely accelerated by the administration of estrogenic compounds.

We have observed that cortisone is effective in suppressing hypercalcuria and hypercalcemia in patients with advanced cancer of the breast. We administered large doses, of 100 to 150 mg., of cortisone daily to five and serum calcium frequently showed rapid return to normal values (Fig. 6). In none of these cases, however, was there any evidence by x-ray examination that bone lesions had diminished. It is also interesting to observe that cortisone in smaller dosages than 100 mg. daily was entirely inadequate to produce such subjective improvement. The mechanism of suppression of hypercalcemia by cortisone is not understood at the present time.

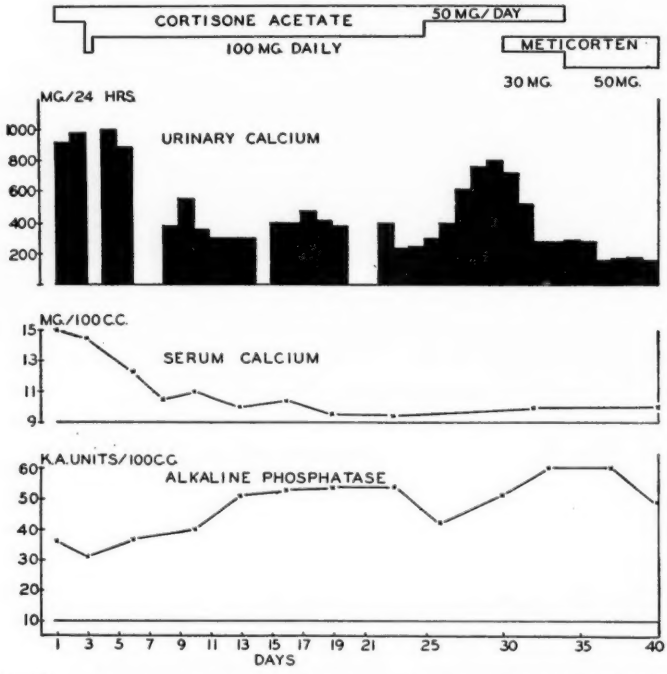


Fig. 6.—Hypercalcemia and hypercalciuria developed in a woman who previously had remission following adrenalectomy. There were changes in urinary calcium excretion and serum calcium after the administration of larger doses of cortisone.

adrenalectomized patients who developed hypercalcuria when relapse occurred. Spectacular symptomatic relief was observed in four patients. There was disappearance of nausea, vomiting, and extreme thirst and sometimes a decrease of bone pain. Patients became alert and no longer were drowsy. In association with symptomatic improvement there was decline in urinary calcium excretion to a normal or near normal level,

COMMENT

We are impressed with the ease with which patients, even those with far-advanced cancer, withstand bilateral one-stage adrenalectomy. This is attributable to attention to details of medical and surgical management, which have been outlined. Adrenalectomized humans maintained on our hormone-substitution program are in excellent health.

It is apparent that profound objective regression of mammary cancer can follow the excision of adrenal glands and that the relief can last for four years, so that it is worth while for such patients to undergo adrenalectomy.

The women with mammary cancer treated by removal of the adrenals alone had, it was thought, no significant ovarian function. They were the patients who either had surgical castration or ovarian irradiation or had passed the menopause long before (7 to 15 years) (Tables 6 and 7). In our laboratory it has been shown that in women in whom

TABLE 6.—*Bilateral Adrenalectomy for Metastatic Breast Cancer*

Status of Ovarian Function	Cases, No.	Objective Response
Surgical castration	15	7
X-ray sterilization	12	5
Spontaneous menopause	7	2
Total	34	14 (41%)

TABLE 7.—*Bilateral Adrenalectomy and Oophorectomy for Metastatic Cancer of the Breast*

Status of Ovarian Function	Cases, No.	Objective Response
Premenopausal	16	8
Spontaneous menopause	16	8
X-ray sterilization	22	7
Hormone-induced menopause	7	2
Total	61	25 (41%)

seven or more years have elapsed since the cessation of menstruation no estrogen can be found in the urine by the bioassay method after adrenalectomy. We are of the opinion, however, that it is most conservative to remove the ovaries of the patients aged 54 or less with advanced mammary cancer who have been selected for adrenalectomy—despite earlier irradiation of the ovaries or extensive and prolonged administration of hormonal substances.

As with all other types of hormonal therapy, relapse often follows remission after adrenalectomy. The failure of bilateral adrenalectomy to produce results in certain cases and the relapse following remissions remain to be explained. Incomplete removal of the adrenal glands or the presence of accessory adrenals may be contributory to the failure of the operation. The adrenal glands are friable and like Swiss cheese in consistency. Any piecemeal technique in removal of the adrenals is apt to leave fragments which are capable of great regeneration. We had one instance in which the left adrenal was removed in pieces, and it was thought at the time of the operation that the gland was all removed. However, six months later, the time of autopsy, 2 gm. of adrenal tissue were found. In this present series we found accessory adrenals in three instances. They were all located along the vena cava and weighed about 0.1 gm. Graham has demonstrated accessory adrenal cortices in the region of the celiac axis in 33 of 100 consecutive autopsies at the Memorial Hospital, in New York.[9] No attempt has been made by us to search for accessory adrenals along the celiac axis during the operation.

We are unable at this time to determine accurately before the operation which mammary cancer is hormone-dependent. Pearson and co-workers have stated that an increased excretion of calcium in urine after the administration of estrogenic substances to patients with osseous metastases indicates an estrogen-dependent cancer.[10] We have found that this consideration is not always operative. The following two conditions may confuse the interpretation: 1. Patients with minimal amounts or even moderate amounts of osseous metastases do not always show increased excretion of calcium in urine. Administration of estrogen in these cases prior to adrenalectomy often fails to alter the excretion level. We found in two instances that the calcium excretion in urine was not elevated in patients with moderate amounts of osseous metastases. No change of excretion level was observed in these two cases after estrogen administration. Both patients responded to adrenalectomy favorably. 2. In patients with a high initial calcium excretion level, further rise in the urinary calcium excretion level after estrogen administration may conceivably be due to continuous progression of the bone destruction, even with-

out estrogen stimulation. In this case the rise of urinary calcium excretion may be mistaken as an indication of estrogen dependency, and adrenalectomy or oophorectomy will not produce any beneficial effects. We found in one instance a rise of urinary calcium excretion after estrogen administration, but adrenalectomy and oophorectomy failed to produce any remission of the disease.

The histological examination of primary tumor has not proved to be entirely reliable in predicting the response to adrenalectomy. At times the regression of mammary adenocarcinoma after adrenalectomy was neither extensive nor prolonged; in a few cases, patients with less-differentiated tumors respond to adrenalectomy favorably. Despite the frailties of morphologic interpretation, we have been able to make prediction in 75% of our cases on the basis of histologic consideration of the type of tumor. It is postulated that the formation of the acini in mammary adenocarcinoma is a positive process directly attributable to secretion induced by hormones. The elimination of critical amounts of supporting hormone from the internal environment of certain cancers alters cell metabolism sufficiently to stop secretion, causing the acini to collapse and cells to shrink, with subsequent involution of the tumor.

SUMMARY AND CONCLUSIONS

Bilateral adrenalectomy or this operation combined with oophorectomy have been carried out in 175 patients with advanced cancer of the breast since May, 1951. The first 100 consecutive cases are the basis for the present report.

The initial operative mortality of 5% has now been reduced to 1.4%. There has been no death in the last 65 cases. No operative morbidity has been observed in adrenalectomized patients.

Medical management in these patients is not difficult. The hormonal substitution regimen employed in this clinic provides safe and adequate replacement in these patients. No postoperative death has been attributable to adrenal insufficiency.

Adrenalectomy has induced significant and prolonged regression of extensive mammary cancers of women who had not responded to earlier treatment with testosterone, estrogen, oophorectomy, and irradiation of the ovaries. Six patients with widely disseminated mammary cancer have had profound regression of the cancer, which has persisted more than 30 months; one woman who had a rapidly advancing mammary carcinomatosis is in good health 49 months after adrenalectomy. The surgical methods are useful therapeutic agents in appropriate cases of cancer of the breast in the human male and female.

The mechanism of regression after adrenalectomy in cancer of the female breast seems to be the withdrawal of critical amounts of hormones similar to those found in the ovary. After adrenalectomy in women who have undergone oophorectomy the excretion of estrogen in the urine is abolished.

Cortisone in the dosage of 100 mg. daily is capable of suppressing hypercalcuria and hypercalcemia in patients with extensive osseous metastases. We have observed remarkable symptomatic improvement, and high levels of serum calcium and urinary calcium excretion often return to normal after cortisone therapy. There is, however, no evidence of actual cessation of bone destruction in these cases.

The use of sex steroids and cortisone in patients who fail to respond to adrenalectomy or to those who have relapse after a remission has not proved to be beneficial to these patients.

We have come to the conclusion that simultaneous bilateral adrenalectomy in a one-stage operation is a practical therapeutic device for selected cases of advanced mammary cancer and that it will provide profound and prolonged relief in a small percentage of patients.

Lorraine Grand provided technical assistance for this report.

REFERENCES

1. Huggins, C., and Bergenstal, D .M.: Inhibition of Human Mammary and Prostatic Cancers by Adrenalectomy, Cancer Res. **12**:134-141 (Feb.) 1952.

2. Huggins, C., and Dao, T. L. Y.: Adrenalectomy for Mammary Cancer: Surgical Technic of Bilateral One-Stage Adrenalectomy in Man, Ann. Surg. **136**:595-603 (Oct.) 1952.

3. Huggins, C., and Dao, T. L. Y.: Adrenalectomy and Oophorectomy in Treatment of Advanced Carcinoma of the Breast, J. A. M. A. **151**: 1388-1394 (April 18) 1953.

4. Lacassagme, A.: Apparition de cancers de la mamelle chez la souris mâle, soumise à des injections de folliculine, Comp. rend. Acad. sc. **195**:630-632 (Oct. 10) 1932.

5. Woolley, G. W.; Fekete, E., and Little, C. C.: Mammary Tumor Development in Mice Ovariectomized at Birth, Proc. Nat. Acad. Sc. **25**:277, 1939.

6. Dao, T. L. Y.: Estrogen Excretion in Women with Mammary Cancer Before and After Adrenalectomy, Science **118**:21-22 (July 3) 1953.

7. Walters, W., and Kepler, E. J.: Surgical Lesions of the Adrenal Glands, J. A. M. A. **111**: 1061-1065 (Sept. 7) 1938.

8. Huggins, C., and Bergenstal, D. B.: Surgery of the Adrenals, J. A. M. A. **147**:101-106 (Sept. 8) 1951.

9. Graham, L. S.: Celiac Accessory Adrenal Glands, Cancer **6**:149-152 (Jan.) 1953.

10. Pearson, O. H.; West, C. D.; Hollander, V. P., and Treves, N. E.: Evaluation of Endocrine Therapy for Advanced Breast Cancer, J. A. M. A. **154**:234-239 (Jan. 16) 1954.

11. Cade, S.: Adrenalectomy for Hormone Dependent Cancers: Breast and Prostate, Ann. Roy. Coll. Surgeons England **15**:71-107 (Aug.) 1954.

12. Cade, S.: Adrenalectomy for Breast Cancer, Brit. M. J. **1**:1-4 (Jan. 1) 1955.

Rupture of Iliac Aneurysm into Duodenum

An Unusual Cause of Upper Gastrointestinal Hemorrhage

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Almost invariably, the concurrence of hematemesis and melena localizes the source of bleeding in the esophagus, stomach, or duodenum. Bockus [4] lists some 50 different or related causes for upper gastrointestinal bleeding. Included in his list is rupture of an aortic aneurysm. This has been of sufficiently rare occurrence to justify reporting such cases in the literature. In 1943, Rottino [12] made a very thorough search of the literature and found 31 cases, adding 1 case. In 1946, Hunt and Weller [8] were able to locate nine more cases. In 1950, Coggeshall and Genovese [5] discovered 8 more reported cases and added 1 of their own, bringing the total number of cases reported in the world literature to 50. Since that time, eight cases were reported by Hirst and Affeldt [7] and other cases have been added by Barrett [3]; Balakian, Ryan, and Perkel [2]; Antzis, Dunn, and Schilero,[1] and Muendel and Pilpel.[11] Therefore, the total number of cases reported of rupture of an aneurysm of the abdominal aorta into the gastrointestinal tract is 62.

Hunt and Weller [8] analyzed their cases and found that there was a 6:1 male-to-female ratio of occurrence and an age range of 20 to 81 years. It is of interest that eight of these patients were 27 to 32 years of age. These authors noted that the most frequent site of rupture of an aneurysm of the abdominal aorta into the gastrointestinal tract, for obvious anatomical reasons, was the third portion of the duodenum. They found that these patients usually had an epigastric mass that was frequently expansile and pulsating and that abdominal or lumbar pain was the chief complaint. Hematemesis and melena were usually observed to be terminal events, but a premonitory seepage could be present for days or weeks. A history of "indigestion" often pointed very suggestively to the possibility of a bleeding peptic ulcer. These authors noted that a high white blood cell count was a constant feature during the period between actual rupture of the aneurysm and death. After rupture, death was found to occur immediately or after a variable period of time. Kampmeier [10] reported, in his review of 73 cases of aneurysms of the abdominal aorta, that in 60% of the cases there was a palpable abdominal tumor mass, and, of those palpable, 98% exhibited expansile pulsations. He also noted that in 75% of cases there was roentgenographic evidence of a calcified mass, a vertebral erosion, or an indefinite soft tissue mass.

Several cases of aneurysm of the iliac artery have been reported in the literature. One case with intraperitoneal rupture and survival after ligation in a 10-year-old girl was reported by Fernbach, Berman, and Cohen.[6] Fatal rectal hemorrhage caused by an aneurysm of the internal iliac artery was reported by Jackman, McQuarrie, and Edwards.[9] No report of an aneurysm of the iliac artery with rupture into the small bowel or duodenum could be found in the literature. At first the suggestion that an aneurysm of the iliac artery could possibly rupture into the duodenum seems incredible, since these two structures are visualized as being in widely separated portions of the abdomen and fixed in their positions. How-

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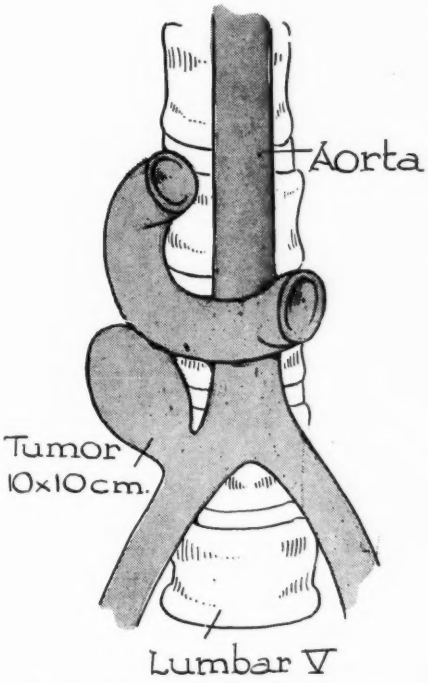


Fig. 1.—Schematic illustration of anatomical relationship between aneurysmal sac and duodenum.

ever, upon closer scrutiny of the anatomical positions of these two structures in the normal person, it becomes apparent that this entity could very well occur. The duodenum is normally 10 to 11 in. in length and assumes the configuration of a *C* or a *U* depending on the length of the ligament of Treitz. The duodenum lies almost entirely in the right one-half of the abdomen, and the third portion crosses the body of the third lumbar vertebra.[13] The aorta bifurcates into the common iliac arteries on the body of the fourth lumbar vertebra (Fig. 1). It is conceivable then that a saccular aneurysm expanding in a cephalad direction for just a few centimeters or a slight variation in the downward sweep of the duodenum could enable an aneurysm of the right common iliac artery to perforate into the duodenum.

The following case of rupture of an aneurysm of the right common iliac artery into the third portion of the duodenum, with resulting fatal gastrointestinal hemorrhage, is presented as an extreme clinical rarity. It is significant not only because of its rarity but because it fits well into the general syndrome of rupture of an aneurysm of the abdominal aorta into the gastrointestinal tract and because of the importance of recognizing this condition as one cause of massive gastrointestinal hemorrhage. With present-day advances in vascular surgery, perhaps in the occasional case, particularly if the aneurysm is of the iliac artery, surgical intervention may be possible.

REPORT OF A CASE

A 68-year-old white man was seen in the admitting room of Confederate Memorial Medical Center at 1:10 a. m. on Oct. 9, 1954. A history was obtained that he had been nauseated for one week and had been vomiting all his food with the exception of breakfast. He had had indigestion 15 years previously, which was relieved by sodium bicarbonate, but he had experienced no recent difficulties. There was also a history of a 35 lb. weight loss over the previous year. During the evening of Oct. 8, he had begun vomiting bright red blood and passing dark red stools per rectum. Blood loss prior to his arrival at the hospital was estimated at 1500 to 2000 cc. When he was first seen, his blood pressure was 140/70 mm. Hg, pulse rate 80, and respiratory rate 30. Mucous membranes were noted to be very pale, and the remainder of the superficial examination was negative. His hemoglobin was reported as 9.5 gm. per 100 cc. During the interview in the admitting room, he vomited several hundred cubic centimeters of blood and passed a similar amount per rectum. He promptly developed a profound shock state. An arterial cut-down was performed, and 1500 cc. of whole blood was given under pressure. Another 1000 cc. of whole blood and 500 cc. of a plasma expander were subsequently given intravenously. An esophageal balloon was inserted, and 1000 cc. of old blood was aspirated from his stomach. He ceased breathing, and an endotracheal tube was inserted and positive pressure oxygen given. His blood pressure was finally obtained at 90/50 mm. Hg, but his pulse rate remained at about 36 per minute. His heart ceased to beat, and he was pronounced dead at 4:30 a. m.

This patient had had one previous admission to Confederate Memorial Medical Center, on Aug. 8, 1954, for symptoms of prostatism and occasional pain in the right costovertebral angle with radiation into the right testis. There was noted on this ad-

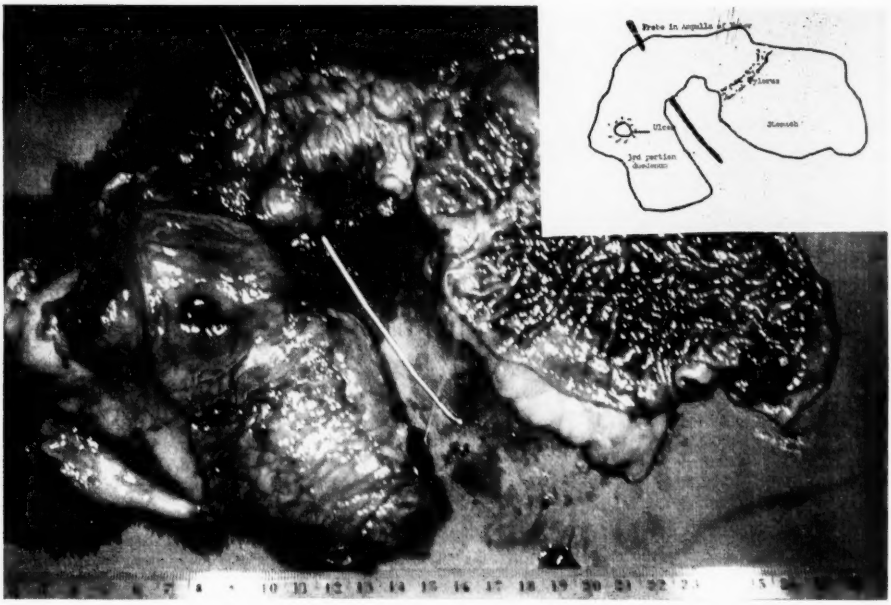
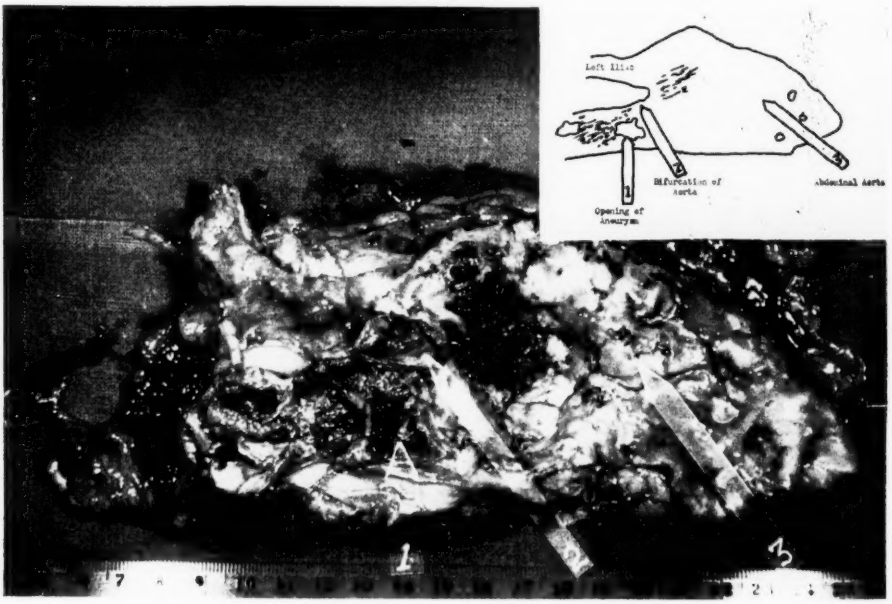


Fig. 2.—Gross specimen illustrating site of perforation in duodenum.

Fig. 3.—Aorta and iliac vessels, posterior view, demonstrating location of aneurysmal orifice in right iliac artery.



mission a questionable pulsating epigastric mass, and the patient subsequently complained both of epigastric pain and of pain in his legs. He responded to conservative treatment and was judged to require no prostatic surgery at that time.

On autopsy the essential findings were confined to the gastrointestinal and vascular systems. The entire gastrointestinal tract was noted to be filled with dark red blood. The duodenum presented a *C* configuration, with the third portion lying somewhat further caudally than is normally seen. The third portion of the duodenum was densely adhered to a 10×10 cm. mass overlying the distal aorta and the right common iliac artery. The aorta and duodenum were removed as a unit, and upon opening the duodenum a 1.5×1 cm. ulceration extending through the duodenal mucosa and wall and entering the mass overlying the aorta was noted (Fig. 2). This ulceration was located 20 cm. below the pylorus and 9 cm. below the ampulla of Vater. It was also approximately 9 cm. from the ligament of Treitz. The aorta was then opened and found to be extensively involved with raised, yellow, arteriosclerotic intimal plaques. A large, irregular opening was discovered in the anterior wall of the right common iliac artery just below its origin from the abdominal aorta. This opening entered the above-described mass, and a friable, irregular thrombus was present in the artery distal to this opening (Fig. 3). On sectioning the mass, it was found to be a true aneurysm almost filled with a laminated thrombus.

SUMMARY

Rupture of an aneurysm of the abdominal aorta into the gastrointestinal tract is a rare cause of massive gastrointestinal hemorrhage, only 62 cases having been reported in the literature. No instance of rupture of an aneurysm of the right common iliac artery into the third portion of the duodenum has been reported. Such a case is presented and an anatomical explanation for its occurrence given. The syndrome of rupture of an aneurysm of the abdominal aorta into the gastrointestinal tract is reviewed.

REFERENCES

1. Antzis, E.; Dunn, J., and Schilero, A. J.: Rupture of Abdominal Aneurysm into Gastrointestinal Tract, Am. J. Med. **11**:531 (Oct.) 1951.

2. Balakian, G.; Ryan, C., and Perkel, C. C.: Gastrointestinal Hemorrhage Due to Ruptured Abdominal Aneurysm, Am. J. Digest. Dis. **17**:408 (Dec.) 1950.

3. Barrett, G. M.: Haematemesis Following Intraduodenal Rupture, Brit. M. J. **2**:319 (Aug. 6) 1949.

4. Bockus, H. L.: Gastro-Enterology, Philadelphia, W. B. Saunders Company, 1943, Vol. 1, p. 559.

5. Coggeshall, W. E., and Genovese, P. D.: Rupture of an Abdominal Aneurysm Associated with Massive Gastrointestinal Hemorrhage, Am. Heart J. **40**:789 (Nov.) 1950.

6. Fernbach, P. A.; Berman, L., and Cohen, B.: Intraperitoneal Rupture of Iliac Aneurysm with Survival Following Surgical Treatment, Ann. Surg. **135**:570 (April) 1952.

7. Hirst, A. E., Jr., and Affeldt, J. E.: Abdominal Aortic Aneurysm with Rupture into Duodenum: Report of 8 Cases, Gastroenterology **17**:504 (April) 1951.

8. Hunt, H. H., and Weller, C. V.: Syndrome of Abdominal Aortic Aneurysm Rupturing into the Gastrointestinal Tract: Summary of the Literature and Case Report, Am. Heart J. **32**:571 (Nov.) 1946.

9. Jackman, R. J.; McQuarrie, H. B., and Edwards, J. E.: Fatal Rectal Hemorrhage Caused by Aneurysm of Internal Iliac Artery, Proc. Staff Meet., Mayo Clin. **23**:305 (July 7) 1948.

10. Kampmeier, R. H.: Aneurysm of Abdominal Aorta: Study of 73 Cases, Am. J. M. Sc. **192**:97 (July) 1936.

11. Muendel, H. J., and Pilpel, M.: Rupture of Aortic Aneurysm with Duodenal Hemorrhage, J. M. Soc. New Jersey **51**:280 (June) 1954.

12. Rottino, A.: Aneurysm of Abdominal Aorta with Rupture into Duodenum: Case Report and Review of Literature, Am. Heart J. **25**:826 (June) 1943.

13. Thorek, P.: Anatomy in Surgery, Philadelphia, J. B. Lippincott Company, 1951, p. 447.

Ischemic Necrosis of the Anterior Tibial Compartment Musculature

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Ischemic necrosis of the muscles of the anterior tibial compartment of the leg occurs only infrequently, but when it does occur permanent impairment of the function of the involved extremity will probably follow. Since this is incapacitating for athletes, soldiers, and many laborers, it is necessary that the surgeon be qualified to make a prompt diagnosis and be prepared to give immediate treatment.

Moretz, in 1953, reported 4 cases of this syndrome which he added to 27 previously reported ones, for a total of 31 reported in English literature up to that time.[1] Some other cases have been reported since, but it is believed that the condition is commoner than this small number indicates. Either a large number are going unrecognized early, or the physician is not seeing the patient until late in the course of the disease, at which time he is including this syndrome with his diagnoses of commoner forms of paralysis. Since no standard form of satisfactory treatment can be determined from previous cases, additional reports may give some clue for better treatment to improve the poor results so far reported.

Only 19 of the cases collected by Moretz could be classed as idiopathic, as the other ones were precipitated by direct wounds or previous vascular disease. To the idiopathic group, we would like to add three patients seen at the U. S. Army Hospital, Frankfurt, Germany, during the past two years, who developed ischemic necrosis of the anterior tibial compartment musculature without trauma or signs of arterial disease.

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REPORT OF CASES

CASE 1.—A 21-year-old soldier was admitted to this hospital on May 7, 1954, complaining of pain in both legs. Onset was acute and occurred approximately 48 hours prior to admission, while patient was walking on a paved street. After onset of pain, it was necessary for him to limp and finally to stop and rest before he could resume walking. Pain in the left leg gradually disappeared, but the pain in the right leg persisted even after he had stopped walking.

On physical examination, all abnormal findings were limited to the right leg. The anterior tibial compartment was tense and extremely tender. There was no redness or other sign of inflammation. He was able to extend and flex the toes but was unable to dorsiflex the foot. The dorsalis pedis pulse was present but was weaker on the right than on the left. Temperature was 99.4 F. Sedimentation rate, urinalysis, and other laboratory tests were within normal limits, except for a slight leucocytosis of 11,400. X-rays of the right lower leg were negative.

He was put on bed rest, and heat was applied to the right leg. However, since heat aggravated the pain, it was discontinued. Aspiration of the anterior compartment on the day of admission produced no pus or old blood. Temperature gradually increased to 101.6 F on the second hospital day, and at this time slight local redness was apparent over the anterior compartment. At the same time it was noted that he was unable to extend the toes as well as the foot. Hypesthesia was present over the dorsum of the foot and between the first and second toes. Repeated aspiration of the compartment was nonproductive. On May 10, a fasciotomy was done. The muscle appeared gray and avascular. No pus or other evidence of infec-

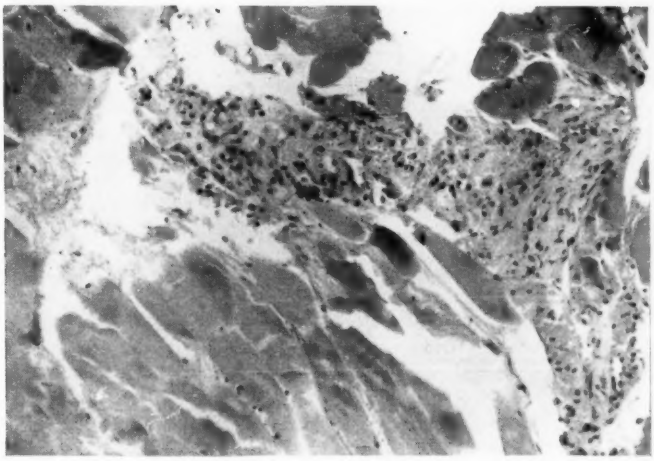

Figure 1

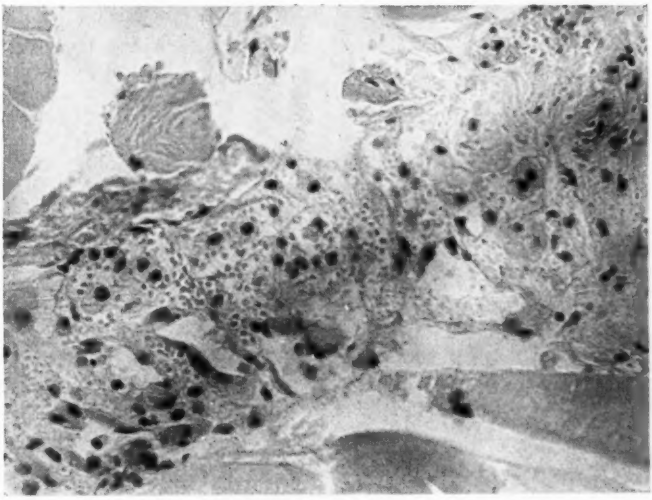

Figure 2

tion was found. On the first postoperative day it was noted that slight muscle power had returned, and the patient's temperature fell to normal. The wound did not heal well postoperatively, so additional débridement was carried out on June 21, 1954, at which time all three muscles of the anterior tibial compartment were found to be necrotic but not infected. Following the second procedure, healing began to take place normally and the patient was returned to the Zone of Interior. At the time of transfer on June 30, 1954, hypesthesia and foot drop persisted and the wound had not completely healed.

Microscopic study of the muscle showed complete loss of differential staining. The interstitial tissue was edematous and contained masses of necrotic debris. One section showed a medium caliber vascular channel which had been occluded by a thrombus. A diagnosis of ischemic necrosis was made. Figures 1 and 2 are representative sections of the muscle.

CASE 2.—A 35-year-old soldier was admitted to the hospital on July 7, 1953, because of pain in the anterior right leg. On the preceding day he had marched for three and one-half hours, after which he noticed pain in his right leg, which gradually

increased until he was unable to walk. There was no history of trauma or infection. He was seen at his local dispensary and given symptomatic treatment without relief and so was transferred. There was no previous history of vascular disease.

On physical examination on admission, the patient was in acute pain. Examination was generally negative except in the right lower leg over the middle third of the anterior aspect, where there was a tender, indurated area. The skin was warm over the area, but there was no redness or other signs of infection. All motions in the knee and ankle joint were very painful. The dorsalis pedis pulse was present bilaterally.

Routine laboratory tests were within normal limits, except for a slight leucocytosis. Repeated x-rays of the right tibia were negative.

The patient was put on bed rest, with elevation and heat to the right leg. However, he had continued tenderness of the anterior muscle compartment and continued swelling and induration until July 14. There was evidence of subcutaneous edema, and hypesthesia was present over the anteriolateral calf. Swelling began to subside, but the induration remained, and a foot drop was noted. On July 29, he was started on physiotherapy, with gradual loss of the induration but with no improvement in the foot drop. On stimulation with both faradic and galvanic current of each of the muscles of the anterior compartment, no response could be obtained. However, some response did return to the great and common toe extensors. There was never any sign of infection.

The patient continued to improve, but paralysis of the anterior tibial muscle continued. He was fitted with a foot-drop brace and discharged to limited duty on Sept. 9, 1953. A follow-up examination was carried out Oct. 15, 1954, at which time there was no tenderness over the anterior tibial muscles but some induration was present. He used his foot-drop brace only rarely, as some fibrosis of the musculature of the anterior tibial compartment had taken place, fixing his foot at the optional position for walking. His range of motion at the ankle was 85 to 95 degrees. The dorsalis pedis pulsation was normal. Electromyogram of the right anterior tibial muscle compartment demonstrated low voltage of 25 to 35μv. This, as compared with 100 to 150μv. on the left, was interpreted by the neurologist as being compatible with an atrophic or diseased muscle.

CASE 3.—A 30-year-old soldier was transferred to this hospital on Sept. 30, 1954, complaining of pain in his right leg and inability to move his foot. On July 12, 1954, under spinal anesthesia he had a high ligation and stripping of varicose veins of the right leg, which he had since 1945. However, none of these were over the tibial compartment. A postoperative infection developed in the superior thigh incision, which limited his activities until Sept. 17, at which time he was sent back to full duty.

On the third day after his return to duty, while doing a great deal of walking, he began to have pain in his right leg and thigh anteriorly and laterally. Pain continued and two days later he found that he was unable to move his right foot. On Sept. 25, he was readmitted.

Physical examination revealed a well-developed and well-nourished man who complained of pain in his right leg and thigh anteriorly and laterally. Swelling and induration were present over the anterior tibial compartment, but there was no redness or other sign of infection. This area was tender and hypesthesia was present over the same area and extended down over the dorsum of the foot. The dorsalis pedis pulse was palpable and equal bilaterally. A foot drop was present, and he was unable to extend the toes or dorsiflex the foot.

Routine laboratory findings were within normal limits. No voluntary motion was elicited in the tibialis anterior, the extensor digitorium longus or brevis, or the extensor hallicus longus. No response was obtained on maximum stimulation with faradic current. Minimum response was obtained on 3 to 4 ma. of galvanic current in each muscle. This was interpreted as indicating destruction of nerve supply plus the majority of the muscle tissue of each muscle.

Treatment consisted of bed rest and paravertebral blocks, with no improvement. On Oct. 10, 1954, a biopsy of the muscles of the anterior tibial compartment was carried out under spinal anesthesia. After incising the fascia, the muscle was found to be gray and necrotic. Bleeding occurred only after superficial and deep biopsy had been taken. The fascia was left open and the skin closed.

Microscopic examination of the muscle biopsy showed the same changes as those seen in Case 1. A diagnosis of ischemic necrosis was made. The incision healed per primam. Pain and tenderness subsided, but hypesthesia and paralysis of the anterior tibial muscle remained. He was ambulated with the aid of a foot-drop brace and returned to the Zone of Interior.

COMMENT

The three cases presented all occurred in young soldiers, the oldest being 36. None of these gave a history or had physical findings suggestive of previous arterial disease. Follow-up on these patients has not shown other arterial disease. There was no direct trauma associated with any case. One soldier

had marched three and a half hours, including frequent rest periods, the day prior to onset of ischemic symptoms, but this was the most strenuous exercise precipitating the syndrome in these three cases.

The symptom complex in all three was similar and follows the typical course, as reported by other investigators. They developed pain and tenderness over the anterior tibial compartment, which was progressive. This did not respond to heat, but symptomatic improvement was brought about by paravertebral blocks. Signs of paralysis of the muscles of the compartment followed with foot drop and inability to dorsiflex the toes. Hypesthesia over the compartment and the dorsum of the foot was a consistent finding. Dorsalis pedis pulsations were present in all three cases. None of the methods of treatment seemed to effect any improvement in these findings, and the signs of paralysis were permanent in all cases.

Of the different methods of treatment, no outstanding one has been found. The first patient had a fasciotomy done on the fifth day of his disease, which demonstrated necrotic muscle that was still sloughing from the incision six months after the operation. The second patient was treated more conservatively with symptomatic treatment and early physiotherapy. The third patient was in the late phase of the disease when transferred here. However, he was given paravertebral blocks and a muscle biopsy was done. The final outcome was the same in all cases. The first patient's course, however, was complicated by the continued sloughing of necrotic muscle after fasciotomy.

The conclusions which can be drawn from these three patients are mainly theoretical. Treatment to be effective must be initiated early. Until more is known about the etiology, symptomatic treatment is certainly indicated. Fasciotomy is of no value if done late after the muscle is already necrotic. From the course of the first patient and in comparison with the other two, it would seem that this is contraindicated as a late procedure, as no rational reason for its use is apparent unless used in the early stages. Since the syndrome is one of ischemic necrosis, it would seem that heat is contraindicated as it increases the oxygen need of muscles already ischemic. On the other hand, it would seem that paravertebral blocks were indicated in all stages of the disease.

Although one patient has been followed for 16 months, none have demonstrated any return of function. Foot-drop braces were helpful when the patient was first made ambulatory, but with healing and fibrosis and later resulting contracture, it is doubted that this is necessary, other than during the immediate postdisease state.

DISCUSSION

It is easy to understand why patients with arterial disease should have necrosis and paralysis below the level of occlusion or spasm of a major artery. It may also be easy to explain why patients sustaining perforating wounds or fractures may have necrosis of adjacent muscles which are also traumatized. It becomes a more complex problem, however, when a young soldier with no other sign of arterial disease, develops paralysis and necrosis of a muscle or group of muscles with no direct trauma.

Since certain points of anatomy peculiar to this group of muscles play a part in the etiology of this syndrome, these factors will be reviewed.

The anterior tibial space, containing the tibialis anterior, the extensor digitorium longus, the extensor hallucis longus, and the peroneus tertius muscles, is almost a closed compartment, bounded posteriorly by the interosseous membrane, medially by the tibia, and anteriorly and laterally by a definite strong layer of fascia which is attached to the tibia and fibula. It is open only inferiorly, at which point the tendons from the muscles enter the dorsum of the foot and are held close to the bone by ligaments which are thickened continuations of the same fascia which covers the muscles. Since the proximal two-thirds of the compartment contain almost all of the muscle bellies, very little if any decompression of the space could be obtained from this inferior opening.

The nerve supply of all these muscles is from the deep peroneal nerve, which descends through the anterior compartment in company with the anterior tibial artery and terminates in the foot, with branches to the extensor digitorum brevis and sensory branches to the skin between the first and second toes.

The arterial blood supply to the compartment muscles is chiefly from the anterior tibial artery which proximally lies deep between the tibialis anterior and the extensor digitorum longus muscles. In the middle of the leg it lies between the tibialis anterior and the extensor hallucis longus, and distally it is crossed by the tendon of the latter muscle after which it is more superficial until it passes into the foot as the dorsalis pedis artery. Throughout its course it is accompanied by its venae comites which join with the posterior tibial vein to form the popliteal. The tibialis anterior muscle is supplied solely by several branches of the anterior tibial artery, whereas the extensor digitorum longus and extensor hallucis longus also received minor branches from other arteries. Variations in the arterial pattern are common and may determine differences in response to vascular interruption.[2]

Although it is well known and easily understood how organs receiving all or the majority of their blood supply from a single artery undergo necrosis when this artery is occluded, one rarely thinks of the muscles of the legs as falling in this category. However, this explanation seems to explain this syndrome. Hughes[3] and Carter,[4] in the study of the pathology involved, found the microscopic sections are similar to those of Volkman's ischemic necrosis and other forms of necrosis due to arterial obstruction. This can be distinguished from necrosis due to venous occlusion or atrophy due to nerve involvement. These pathological findings definitely indicate lack of arterial blood supply as the causative factor. Although almost all reported cases have had hypesthesia over the areas supplied by the deep peroneal nerve, this is believed to be also due to ischemia as a result of the same process, rather than an etiological factor.

Carter did oscillometric determination on four of his nine cases. Oscillations were decreased in one but were increased in the other three. He also did arteriography on five cases. In each case there was no abnormality noted in the major vessels, and good filling was obtained in all. Almost all reported cases have had good dorsalis pedis pulsation.

In order to compromise the above information and the fact that the dorsalis pedis pulse is usually palpable with the theory of arterial occlusion as the cause of the syndrome, it must be remembered that the arterial pressure gradient falls greatly from major arteries down to the arterial limbs of capillaries which supply the muscle. Whereas, a systolic pressure of 100 mm. of Hg may be present in the dorsalis pedis, the pressure in the arterioles supplying the muscles is normally down to 40 mm. of Hg.[5] Thus, it is possible to occlude the blood supply to the muscles without occluding the dorsalis pedis pulsations.

With this in mind, Carter's theory of etiology is most reasonable and probably explains the majority of cases.[4] He believes that sudden or strenuous use of this group of muscles results in the rupture of muscle fibers, causing hemorrhage and edema which produces so much tension in the rigid compartment that the capillary blood supply is occluded and necrosis results. He believes that the neurological findings are also due to ischemia.

The diagnosis usually presents no problem. Although the three cases presented from this hospital gave practically no history of trauma, the usual patient gives a history of onset at a time when he was engaged in a long march, was playing in a competitive sport, or was otherwise subjected to trauma or stress to this area. The onset may follow such exercise by a day and may be insidious, although the pain is usually severe and the onset acute. It begins with pain and tenderness over the anterior tibial compartment.

which may subside if the exercise is stopped with the onset of symptoms. If exercise is continued, the pain becomes worse, swelling is noted over the compartment, which becomes hard to palpation, and signs of paralysis of the muscles of the compartment and the extensor digitorum brevis muscle develops. There may be hypesthesia over the dorsum of the foot, with anesthesia between the great and second toe.

The differential diagnosis includes cellulitis, osteomyelitis, thrombophlebitis, and deep abscess in the compartment. However, a negative x-ray and the lack of other signs of inflammation are usually sufficient to eliminate the other possibilities. Occasionally the patient may develop a low-grade fever, but there is rarely any redness or local heat.

TREATMENT

If the syndrome is seen in the late stages, complete destruction of the muscles will already have taken effect and the process will be irreversible. Therefore, early diagnosis and prophylactic measures are of the utmost importance. The majority of the reported cases have occurred in servicemen, and practically no cases have been reported from trained or professional athletes. Therefore, it would seem that a graduated training program would be less likely to produce the syndrome than the occasional long march or a contest in which the contestants had not gone through a graduated training program. If pretibial pain develops during exercise, it is important that a serious view be taken and further exertion prohibited for several days. At this stage the process is reversible and can usually be adequately treated by bed rest, elevation, and close observation.

If the process continues and hardness, swelling, and tenderness develop with foot drop or other signs of paralysis of this group of muscles, the person should be immediately hospitalized, as an emergency measure. Just as in other forms of arterial occlusion, the first few hours are of the utmost importance. At this stage very little hope of preventing permanent foot drop can be offered the patient with the use of conservative measures alone. From the discussion concerning the etiology, it is evident that the only effective treatment would be an early decompression. This must be done by means of a long fasciotomy before necrosis has occurred. Repeated paravertebral blocks are indicated to reduce accompanying arterial spasm.

The only reported case of recovery after paralysis had occurred is reported by Sirbu and co-workers,[6] who did bilateral fasciotomies on a patient who developed the syndrome bilaterally after a long march. The patient regained use of the muscles on the left, while those on the right went on to complete necrosis. Whereas, the duration of symptoms in this case was four days, it would seem that the first 24 hours would be the optimal time. Very few cases are seen during this critical period, and, therefore, the golden opportunity for prevention of permanent disability is missed. If wider publicity could be given the signs and symptoms of this syndrome and the necessity for immediate hospital care, excellent results should be obtained.

Fasciotomy done late is not recommended, as too many reported cases have followed the same course of our Case 2. Continued slough has occurred, necessitating prolonged hospitalization. Local heat is not recommended early, as the necrosis may be made more extensive by the application of heat to an already ischemic muscle. Neither are generalized vasodilators indicated, because of the danger of decreasing the blood flow to the muscles as a result of the generalized vasodilitation in the skin.

SUMMARY

Ischemic necrosis of the anterior tibial compartment musculature occurs probably much more commonly than is recognized, and when it does occur permanent impairment results. Three such cases seen within a two year period are reported. The most

plausible theory of etiology is discussed and the diagnostic physical findings are mentioned.

Just as in other conditions of arterial occlusion, the first few hours of treatment are of utmost importance. Whereas rest and conservatism may be used if pain is the only symptom, wide fasciotomy and paravertebral blocks must be done immediately if paralysis of these muscles has occurred.

REFERENCES

1. Moretz, W. H.: The Anterior Compartment (Anterior Tibial) Ischemia Syndrome, Am. Surgeon **19**:728-749, 1953.

2. Edwards, E. A.: The Anatomic Basis for Ischemia Localized to Certain Muscles of the Lower Limb, Surg. Gynec. & Obst. **97**:87, 1953.

3. Hughes, J. R.: Ischaemic Necrosis of the Anterior Tibial Muscles Due to Fatigue, J. Bone & Joint Surg. **30-B**: 581, 1948.

4. Carter, A. B.; Richards, R. L., and Zachary, R. B.: Anterior Tibial Syndrome, Lancet **2**:928, 1949.

5. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice: A Text in Applied Physiology, Ed. 2, Baltimore, Williams & Wilkins Company, 1950, p. 143.

6. Sirbu, A. B.; Murphy, M. J., and White, A. S.: Soft Tissue Complications of Fractures of the Leg, California & West. Med. **60**:53, 1944.

Metabolic Derangements Imperiling the Perforated Ulcer Patient

I. The Dehydration and Fluid Shifts

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Abundant evidence has accumulated in recent years to indicate that surgical diseases and operations give rise to widespread and significant metabolic derangements.* A number of conditions have been investigated, and a general pattern is emerging, but the differences between individual conditions or operations which may be of significance to therapy are not fully apparent. Only in a few areas, such as burns and fractures, has a single entity been studied repeatedly, and in both of these extensively investigated conditions the variations within the group are wide. To date the experience with the metabolic changes of surgical disease might be called horizontal. Five years ago it occurred to us that it would be valuable to take a more vertical view, studying one entity sufficiently often to encounter most of the variables. We hoped this type of investigation would enable us to describe with authority any common pattern which emerged and would lead to a more secure plan of therapy.

The basic requirement for selection of the surgical condition to be studied was that it should be a disease entity with a relatively uniform pattern of injury from patient to patient. The consequences of the perforation of a peptic ulcer fulfilled that requirement.

Three other factors also entered into the selection of perforated ulcers: the active controversy as to the management of the perforation, the high mortality rate irrespective of the therapy chosen, and the probable similarity of the injury to that of a cutaneous burn. At present three modes of therapy for perforation have enthusiastic supporters, and no agreement exists as to which treatment should be employed. The conservatives avoid surgery, the middle-of-the-road surgeons advocate simple closure, and the more radical would add immediate subtotal gastrectomy. Each method of treatment involves a risk.

Simple closure is relatively well tolerated if performed early, and it prevents extension of the chemical peritonitis by sealing off the perforation through which the irritating peptic juices escape. The risk of this operation increases, however, as the interval between perforation and operation lengthens.†

The decision to go beyond the immediate closure of the perforation, adding subtotal gastrectomy, offers the possibility of a

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From the Department of Surgery, Harvard Medical School, and the Surgical Services, Massachusetts General Hospital.

* There are numerous papers covering this field of interest. Those cited constitute a small but representative fraction of the existing literature on metabolic effects of surgical disease. References 1-12.

† References 13-19.

healthier future at the risk of a more hazardous operation.

The conservative, nonoperative approach is based in part upon the concept that the likelihood of spontaneous sealing of the perforation increases with the passage of time. A more important reason for abandoning operative therapy, however, is that the patient who suffers from this form of peritonitis sickens rapidly and after a few hours withstands operation poorly.

The mortality rate regardless of therapy is high. DeBakey reported an over-all mortality of 23.7% in 2746 cases studied in 1939.[22] In the literature, widely different mortality statistics are found for each of the three current methods of therapy. Death rates from 84% to 0% are given for nonoperative management, from 65% to 2% for simple closure, and from 29% to 0% for gastrectomy.‡ A review of 289 perforations in this hospital between 1940 and 1951 revealed an operative mortality of 4% and a fatality rate of 41% in patients not operated on.[29] A multiplicity of factors, including selection of cases, availability of antibiotics during the study, and postoperative management, make comparison of mortality figures from different clinics and different periods unsatisfactory.

Because the problem of therapy cannot be settled by mortality statistics and because of the continued high mortality, it is evident that further investigation into the factors contributing to the deterioration of the perforated ulcer patient is needed. Some of the confusion about the choice of therapy might be dissipated if we knew more about the metabolic derangements and nutritional deficits contributing to that deterioration. Our selection of ulcer perforation for study was based in part on the hope that our findings might not only be informative regarding injury and operation in general, but that they might lead directly to improvement in the management of the perforated ulcer patient and those with other intestinal injuries and perforations.

‡ References 18-28.

The perforation itself is a wound of minor importance. It is the insult of peritoneal contamination with gastric juices which constitutes the real injury, a chemical burn. The area of the peritoneal surface involved is probably wide enough to be equivalent to a skin burn of a moderate extent. This comparison with a cutaneous burn is an obvious one and suggested the probability that the same methods of study which had contributed so much to the understanding of burn shock might yield valuable information about the effects of peptic ulcer perforation and any subsequent operation as well.

The study has confirmed the anticipations both in uniformity of findings and in similarity of the metabolic and nutritional changes to those seen in burned patients.

PLAN OF STUDY

Material.—To insure an adequate view of the pattern of injury and its complications, the study included 24 patients. There was no selection of cases. The patients were consecutive in so far as the surgical metabolic unit and the laboratory were able to accept patients for study. Treatment included simple operative closure in 23 cases. The interval between perforation and arrival at the hospital averged three hours and nine minutes. There were no primary resections. The anesthetic agents employed were ether and nitrous oxide in 21 cases and spinal tetracaine (Pontocaine) in 2. One patient was managed conservatively without operation. He did not reach the hospital until 11 hours after perforation. Twenty of the patients ran relatively uncomplicated courses. Four required secondary operations. There were no deaths. Chance dictated that all the patients should be men. No females with perforated ulcers presented themselves for admission to the hospital during the period of our investigations. The age range was from 31 to 69 years, the average being 48. The patients' average weight on admission was 57.8 kg. (127.2 lb.). The location of the ulcer was duodenal in 15 cases, gastric in 8, and undetermined in 1, the case without operation.

The operative and postoperative management was that which was current in this hospital at the time and was ordered and carried out by the resident staff. The blood pressure was determined on entry, every 5 to 10 minutes during the operations, and every half hour for 8 to 12 hours thereafter. Postoperative treatment consisted of sedation, nasogastric suction, and intravenous dextrose, saline, and whole blood as needed. No plasma was given. Although the fluid therapy varied from patient to

patient, on the average the patients received during the first three days a total of nearly 7000 cc. of nonelectrolyte dextrose solution and 3500 cc. of saline. Throughout this period all were on continuous nasogastric suction and were given only sips of water by mouth. The adequacy of the fluid therapy was judged by means of the urinary output. Thirteen patients were transfused either at operation or when the degree of anemia present warranted whole blood therapy. On request from the research team supplementary nitrogen, potassium, and phosphorus were given in special cases. Gastric drainage was discontinued and oral feeding resumed between the third and eighth days after perforation at the discretion of the surgical resident. The time of ambulation was not fixed.

Investigative Routine.—The investigative routine was oriented to observe any shift in water, electrolytes, or nitrogen which might occur within the body or between the body and its environment as a result of the peritoneal irritation following perforation or as a result of operation and the subsequent surgical care. From the moment of admission to the hospital until the day of discharge the patients were kept under metabolic scrutiny. Immediately after establishment of the diagnosis, and prior to the onset of fluid therapy in the majority of the cases, the patient was weighed, blood samples were drawn for serum protein and electrolyte determinations, and an indwelling catheter was inserted in the bladder. The volume and specific gravity of the urine were measured hourly until good renal function was assured and the adequacy of the rate of therapy established.

A special effort was made to collect the urine excreted between the time of perforation and the onset of fluid therapy. It seemed likely that in this period before correction of the patients' dehydration any shifts of electrolytes from the cells to the extracellular fluid and from the extracellular fluid through the kidneys to the urine would be most easily observed. Thereafter all urine, feces, vomitus, and gastric drainage were carefully collected for quantitative analysis. In four cases fluid aspirated from the peritoneal cavity at operation was also saved for study. The only unrecorded fluid shifts between the patients and their environment were losses through the skin and respiratory tract. To assure adequate records of fluid intake and output, patients were moved immediately after operation to the surgical metabolic ward, under the supervision of a specially trained metabolic nurse.

The shifts of water within the body were measured directly by repeated determinations of the extracellular fluid and plasma volume and indirectly by measurement of changes in the hematocrit value and the electrolyte and protein concentrations of the blood serum. Preoperative determinations of the plasma volume and the extracellular fluid volume were carried out soon after admission. The measurements were made before fluids were administered, unless the patients were sufficiently ill to make immediate fluid therapy mandatory.

The electrolyte shifts within the body and losses from it were also studied by observing the total electrolyte balances. To separate the shift of ions due directly to redistribution of water in the body compartments from that due to secondary metabolic derangements, comprehensive metabolic studies were made.

This first paper reports the dehydration which follows on the heels of the perforation. The shifts in electrolytes and nitrogen are dealt with in three subsequent papers.§ Changes in metabolic rate and in eosinophile count are described in the fifth paper,[33] and the plan of therapy is presented in the sixth.[34]

METHODS

The plasma volumes were measured by the dilution of Evans blue dye (T 1824).[35] The red cell volume was calculated from the plasma volume and the large-vessel hematocrit value. The thiocyanate and sodium spaces were measured 50 minutes after injection of thiocyanate and radioactive sodium ions (Na^{24}).‖ The normal values for these volumes have been found in this laboratory to be as follows:[38]

Thiocyanate space	18.0-25.0% body weight
Sodium space	18.0-25.0% body weight
Plasma volume	3.5- 4.5% body weight
Red cell mass	3.0- 4.0% body weight

OBSERVATIONS

1. Hematocrit Changes: Initial Hemoconcentration and Subsequent Dilution with Fluid Therapy

Changes in the hematocrit values were followed in 23 patients. In general, measurements were made once or twice a day on the day of perforation and the first postoperative day, daily for two or three days thereafter, and then at gradually increasing intervals. On admission nine patients had hematocrit levels above 50%. In only two cases (Cases 9 and 20) were subnormal levels encountered, and in those cases hemoconcentration was almost certainly masked by a preexisting anemia. Although levels of 42% to 50% are accepted as normal

§ References 30-32.

‖ References 36 and 37.

for the hematocrit value in the male, in patients with peptic ulcers downward deviations due to anemia are to be expected. Hematocrit values above 50% may be considered clear-cut evidence of vascular dehydration. The hematocrit changes of the first 10 patients studied are shown in Chart 1*A*.

After admission the hematocrit levels fell in 20 of the 23 cases. This drop coincided with the administration of parenteral fluids. The 3 patients whose hematocrit values rose were among 10 who were transfused early. On the first, second, and third postoperative days the average hematocrit levels were falling slowly through the normal range. The subsequent course of the hematocrit values depended upon the status of each patient from the standpoint of nutrition, sepsis, and anemia. Eleven patients showed levels below 41% near the end of the first week. Transfusions were given as indicated, and the hematocrit levels gradually returned to normal.

2. Changes in Serum Protein Concentration: Additional Evidence of Early Hemoconcentration

The patients showed high normal or abnormally high serum protein concentrations on admission, preexisting nutritional deficits notwithstanding.¶ Admission concentrations measured in 13 cases averaged 6.9 gm. per 100 cc., with a range from 6.5 to 7.8 gm. (Chart 2). With the administration of fluids, the serum protein concentration fell. On the day after perforation the average level had reached 6.3 gm. per 100 cc., and by the third day it had fallen to 6.05 gm. In nine of the cases drops below 6 gm. per 100 cc. were observed, and in one the concentration fell to 4.5 gm. The lowest concentrations were measured on the fourth and fifth days after operation, after which the levels rose slowly to normal.

¶ Serum electrolyte concentrations were also intially high, the serum chlorides exceeding the normal range.

3. Extracellular Fluid Volume Changes

The volume of the plasma portion of the extracellular fluid was measured in 21 patients. In 18 repeated determinations were made, but in the remaining 3 only a single measurement was made, on the day of perforation. In all 21 of these cases the volume of fluid in which sodium thiocyanate ions are distributed after injection was also measured, and in 10 the volume of the radioactive sodium space was determined as well. The changes in all patients tended to follow a typical pattern in the early days, but in two cases observed throughout the subsequent development of complications secondary changes were encountered.

A. The Plasma Volume.—(1) Initial Contraction: Initial plasma volume determinations were made before any appreciable amount of fluid had been given in 10 of the 21 patients whose plasma volumes were measured. Six of these volumes were smaller than normal.# Four of the eleven patients who received fluid therapy before the first measurement also showed an initial reduction in the volume of plasma. In 12 patients, including 6 of those measured before treatment, two determinations were made within the first 36 hours after perforation. A reduction in plasma volume occurred between the two measurements in 4 of the 12 cases (Charts 3*A* and 3*B*). The average fluid intake in the interim was 2154 cc. This group of four included two of the patients who had failed to show contraction of the plasma volume before fluid therapy. These two patients were among those reaching the hospital relatively soon after perforation (one, and two and one-fourth hours). A fifth patient showed no alteration in plasma volume during the early hours.

(2) Subsequent Expansion with Fluid Therapy: In the remaining seven patients whose volumes were measured twice in the first 36 hours, expansion occurred. These

Since the "normal" volumes were calculated on the basis of the low admission weights, these decreases in plasma volume were all the more significant.

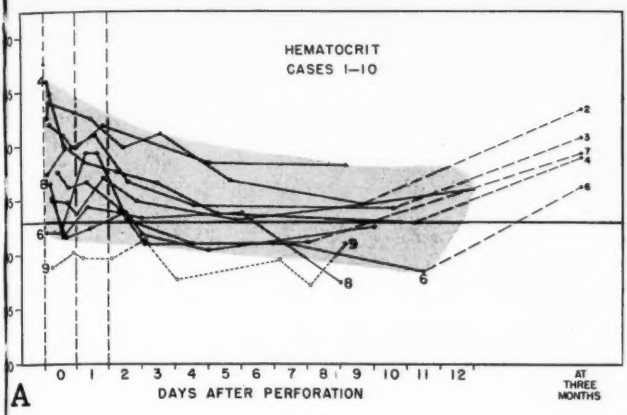

Chart 1 *A*.—Evidence of hemoconcentration in the traumatized patient. Elevation of the hematocrit value due to early dehydration in the perforated ulcer patient. The dotted line, the lowest, shows the levels of a patient with preexisting anemia. This patient gave a history of at least one massive gastrointestinal hemorrhage prior to perforation. Another hemorrhage occurred on the 10th postoperative day, necessitating subtotal gastrectomy.

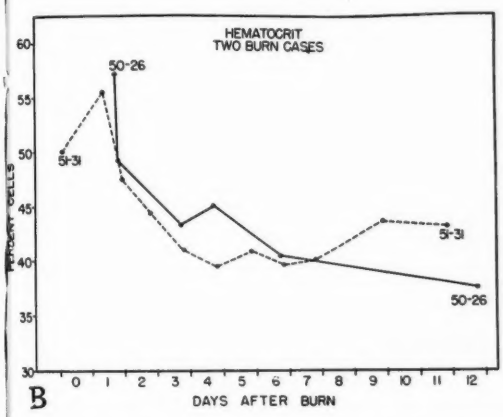

Chart 1 *B*.—Evidence of hemoconcentration in the traumatized patient. Elevation of the hematocrit value due to early dehydration in burns of moderate severity. Case 51-31, a 34-year-old man, had burns of 10% of his body surface (1% of third degree). In Case 50-26, an 82-year-old woman, the extent was 20%; 8% was of full thickness.

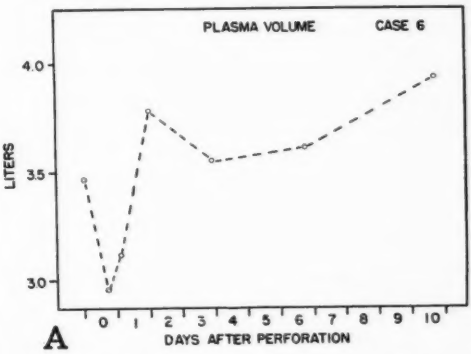

Chart 3 *A* (Case 6).—Contraction of the plasma volume after ulcer perforation; reexpansion with fluid therapy. The plasma volume changes. Despite administration of 2942 cc. of fluid in the 18-hour interval between the first and second blood volume measurements, the plasma volume of this patient diminished. When an increase in the rate of fluid administration in the next nine hours brought the total intake to 5400 cc., the plasma volume began to reexpand.

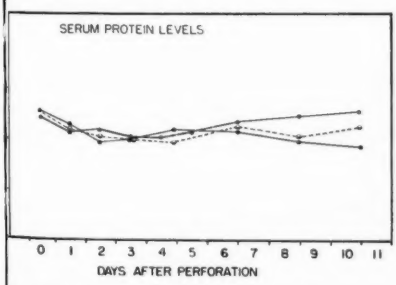

Chart 2.—Elevated initial serum protein concentration and subsequent fall as dehydration is relieved by fluid administration. The open circles indicate protein concentration in patients receiving a nitrogen intake and the filled circles the protein concentration in patients receiving a moderate or nitrogen intake. Parenteral nitrogen therapy not prevent the drop in serum protein concention. The effectiveness of intravenous amino therapy in preventing nitrogen loss is discussed the paper on nitrogen.[32]

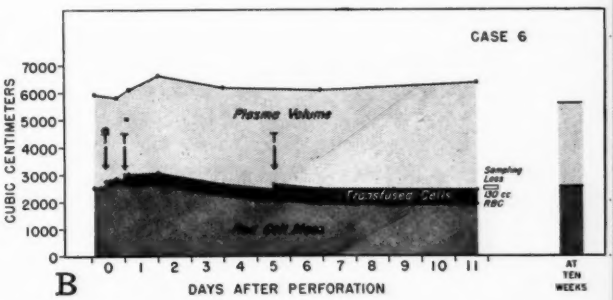

Chart 3 *B* (Case 6).—Contraction of the plasma volume after ulcer perforation; reexpansion with fluid therapy. Whole-blood volume and red-cell mass changes. In addition to requiring fluids to restore his plasma volume, the patient also needed three whole-blood transfusions, indicated by the arrows, to maintain his red-blood-cell mass.

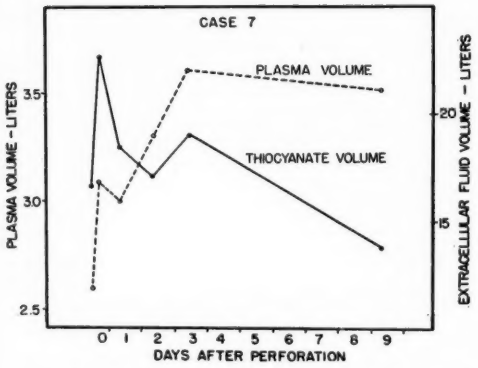

Chart 4 (Case 7).—Initial contraction of plasma volume and expansion of the thiocyanate volume after trauma; subsequent expansion of both with hydration. On admission this patient had a subnormal plasma volume and a greater than normal thiocyanate volume; both spaces expanded with fluid therapy.

patients had an average fluid intake of 3208 cc. (Chart 4). As the quantity of infused fluid increased, reexpansion eventually occurred in all 18 of the patients on whom repeated determinations were made. The average volume increase was 0.6 liters, with a range from 0.2 to 1.6 liters.

B. The Interstitial Fluid Volume.—(1) Initial Expansion: At the time when the plasma portion of the extracellular fluid was contracted, the total extracellular fluid volume was expanded (Chart 4). On the day of perforation, thiocyanate volumes were measured in 20 of the cases treated surgically, 4 of them also having radioactive-sodium-space measurements. The thiocyanate volumes averaged 16.1 liters, exceeding the patients' expected normal spaces by 3 liters.* The average sodium spaces showed a 2-liter increase over the expected volume.

(2) Further Expansion with Therapy: Coincident with the reexpansion of the plasma volume, the already expanded thiocyanate and radioactive-sodium volumes increased still further (Charts 5*A* and 5*B*). Peak volumes were reached at intervals from 4 to 64 hours after perforation, the average being 28 hours. Owing to the irregu-

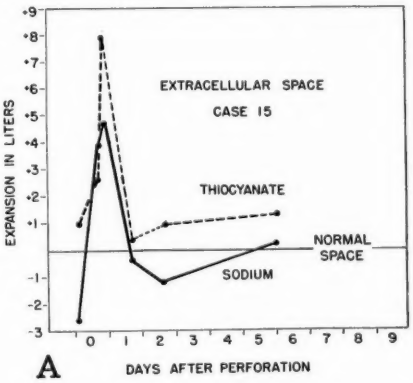

Chart 5 *A* (Case 15).—Expansion of the extracellular fluid volume after perforation. Sodium and thiocyanate spaces in a patient whose course was uncomplicated. The extracellular fluid volume, as measured by thiocyanate and radioactive sodium ions, increased during interstitial edema formation and during rehydration of the initially depleted plasma volume. Contraction to normal accompanied wound healing and recovery.

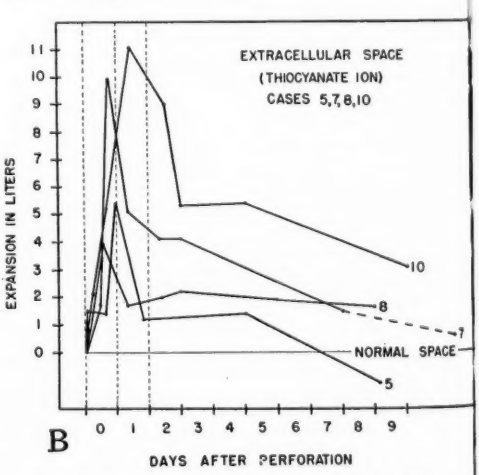

Chart 5 *B*.—Expansion of the extracellular fluid volume after perforation. Thiocyanate spaces in four other uncomplicated cases. The increase in thiocyanate volume was rapid and exceeded clinical estimates of the volume of edema. The subsequent contraction of the thiocyanate space took place more slowly.

* The expected volumes are calculated from the patients' admission weights, assuming the volume of extracellular fluid in liters to be equal to 22% of the body weight in kilograms. We have found that in normal subjects the volumes of the thiocyanate and sodium spaces are close to that percentage of body weight uncorrected for specific gravity of the fluids involved.

lar availability of Na^{24}, insufficient data were collected to permit averaging of the sodium-space expansions, but peak volumes of 19, 21, and even 24.5 liters were obtained. Sodium-space expansions greater than 4 liters were encountered in 6 patients, and the thiocyanate expansion exceeded this range in 19 cases. The average of the peak thiocyanate spaces of 21 cases reached a volume of 20.6 liters, 4.5 liters above the average admission volume and 7.4 liters in excess of the expected size of the extracellular fluid space (range, 2.9-11.9 liters).† The measured increases between admission and peak thiocyanate concentrations were greater than 6 liters in five cases and more than 4 liters in three others. These expansions are too great to be explained by the experimental error inherent in the thiocyanate and sodium methods.

(3) Final Contraction: After the rapid initial expansion the thiocyanate volume contracted slowly toward normal in patients in whom wound healing and recovery were progressing satisfactorily (Chart 5). Final volumes obtained during the second week after perforation in 15 cases averaged 16.1 liters, or 28.3% of their body weights. Four patients, whose spaces were measured three to six months after recovery, showed a subsequent further drop of from 1.1% to 3.5%. It should be emphasized that a smooth pattern of initial expansion and subsequent contraction of the thiocyanate space was not obtained in all cases. Many unexplained drops and rises occurred.

† Evidence that the apparent extracellular-fluid-space expansion is not an artifact due to use of the patients' low admission weights as a basis for calculation of the expected normal spaces is found by substituting 15.4 liters, the normal extracellular fluid volume of a 70 kg. man, as a base line. The average expansion then becomes 4.9 liters, with a range from 0.9 to 8.4 liters.

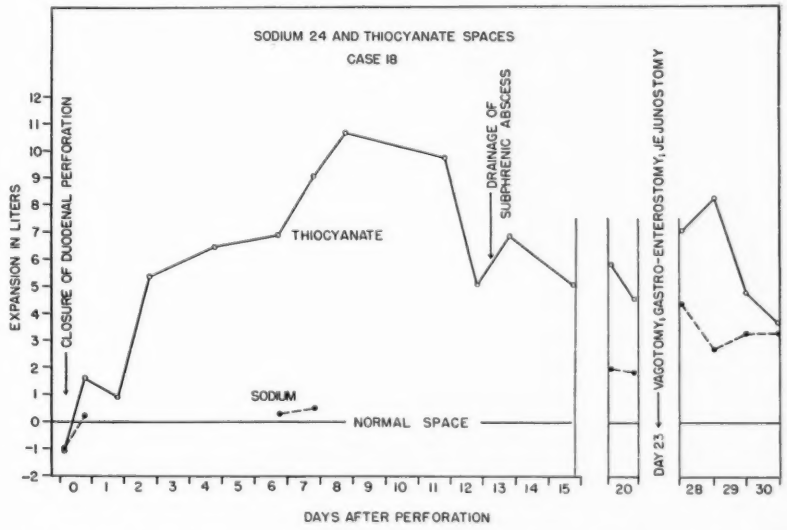

Chart 6 (Case 18).—Prolonged elevation of thiocyanate space in presence of sepsis; secondary elevations with additional trauma. The patient developed a subdiaphragmatic abscess which was drained on the 13th day. Gastroenterostomy, vagotomy, and jejunostomy were performed 10 days later because of pyloric obstruction. The thiocyanate space increased with sepsis and after each operative procedure. The difference between the sodium and thiocyanate spaces is statistically significant, but it is not understood. Different cell membrane permeabilities to the two ions during sepsis or differences in protein-binding characteristics may account for the discrepancy.

C. Secondary Expansions in Patients Developing Complications.—In two of the four patients whose recovery was delayed by complications requiring additional surgery, the return of the extracellular fluid volume to normal was deferred. In one of the two, Case 23 wound dehiscence and operative closure were followed by a secondary expansion of both spaces. Four days after the procedure the thiocyanate volume reached 27.2 liters, the largest expansion observed in any case. Radioactive sodium was not available at the time of the second thiocyanate peak, but on the preceding day a determination showed a rise to 20.7 liters. In the second patient, Case 18, the thiocyanate space, instead of reaching a peak in the first day or two after perforation, expanded steadily for the first nine days (Chart 6). This rise coincided with the development of a subdiaphragmatic abscess. While the thiocyanate volume soared to 10 liters above the expected extracellular space, the radioactive sodium volume failed to do so. Essentially normal volumes of 11.3 and 11.5 liters were observed on the eighth and ninth days, when the thiocyanate volumes were 17.9 and 20.1 liters. The difference between the two spaces is well beyond the limits of error of the two methods. A second minor rise in thiocyanate volume followed surgical drainage of the abscess, and a third operation, for pyloric obstruction, 10 days later brought about a third expansion.

4. The Fluid Balance

A. Intake.—The volume and nature of the fluids administered varied from case to case, but on the average the patients received 1125 cc. of saline and 2400 cc. of dextrose in distilled water during the first 24 hours. Ten received whole blood in addition (averaging approximately 500 cc.), and six were given 50 to 100 cc. infusions of a solution containing potassium and phosphate ions as well (Paper II in this series [30]). On the second and third postoperative days the water and saline intakes were slightly lower than the preceding day, averaging 1.9 and 1.8 liters of dextrose in distilled water and 1.0 and 0.8 liters of dextrose in saline. Thereafter intravenous intakes decreased and oral intakes increased according to the tolerance of the patients.

B. Output.—(1) Urinary Fluid Losses—Initially Scanty Outputs Increasing on Fluid Therapy: Urinary outputs were measured in 18 patients. On admission the volume was scanty. The hourly rates of excretion prior to catheterization on entry were calculated whenever the patients were able to state the time of last voiding with certainty. Reliable information was received in 14 cases. Eleven were excreting less than 40 cc. per hour. Of these, seven had an hourly excretion rate of less than 30 cc. and four, less than 20 cc.

During the early hours after admission, urinary outputs continued low. The single patient treated without operation excreted no urine whatsoever for the first three and a half hours. Ten of the eighteen patients operated on put out less than 40 cc. an hour in the first three hours after admission; eight excreted less than 30 cc.; four, less than 20 cc., and two, less than 10 cc., all of these in spite of intravenous therapy of from 62 to 263 cc. per hour.

With continued fluid therapy, however, the urinary volume rose. Outputs close to 1400 cc. were observed daily after the day of operation except on the second and fifth postoperative days. A mild diuresis averaging 1673 cc. was observed on the second postoperative day, and an output only slightly smaller (average, 1651 cc.) was seen on the fifth day.

(2) Gastric and Duodenal Losses: During the three-day period of complete restriction of oral intake, gastric drainage and vomitus in our patients totaled from 80 to 3298 cc. per 24 hours, the daily average being 688 cc. With resumption of oral intake on the third postoperative day, suction drainage was discontinued, and either gravity drainage or intermittent aspiration was substituted. On this regimen and on fluid intakes increasing slowly from 30 cc. of water per hour the average gastric output remained high through

the third postoperative day (686 cc). The outputs fell to an average of 441 cc. on the fourth postoperative day, and by the following day half of the patients were showing so little gastric retention that their tubes were removed. Gastric losses were prolonged in four patients with partial pyloric obstruction and also in the single case without operation.

(3) Peritoneal Fluid Losses: The volume of fluid aspirated from the peritoneal cavity at the time of operation was not large. In four cases as much fluid as possible was removed by aspiration. The volumes were 38, 125, 200, and 410 cc. The protein concentration of this fluid was in the vicinity of 4.6 gm. per 100 cc.

C. The Balance.—During the day of operation and the first two postoperative days, the fluid balances of all but 3 of the 18 patients for whom data are available were persistently positive. The volume of fluid retention was small, however, (daily average, 1.8 liters) and has not been corrected for respiratory or skin losses, which would swing the balance to the negative side in at least three additional cases and possibly more.‡ Fluid balances for the succeeding days showed an uncorrected average daily positive balance of 1 liter.§

Adequate fluid balance data are available in 13 cases whose thiocyanate volumes were measured repeatedly. Peak volumes in these cases averaged 20.2 liters, 7.1 liters above the expected normal volumes. The fluid retention between perforation and peak thiocyanate expansion in these cases averaged only 2.3 liters, 4.8 liters short of the apparent extracellular expansion (Charts 7*A* and 7*B*).

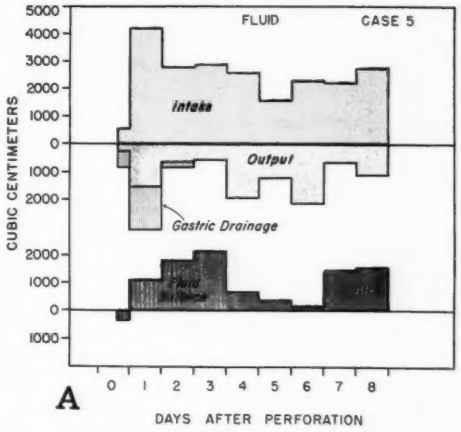

Chart 7 *A* (Case 5).—Inadequacy of fluid intake as a source of water for extracellular fluid space expansion. Too small a positive balance to account for thiocyanate space expansion. The patient's intake had exceeded his output by 1 liter at the time when his thiocyanate space had increased by 5 liters (Chart 5*B*).

In only two cases could exogenous water account for the apparent increase in volume of the extracellular fluid. In 11, fluid balances fell short of the measured expansion by 0.1 to 9.4 liters. Fluid balances in two cases were actually negative at the time of peak expansion.

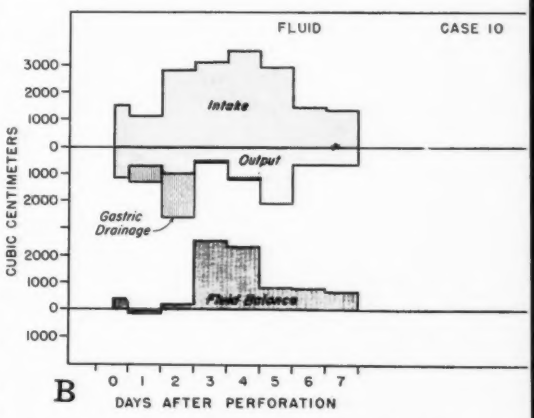

Chart 7 *B* (Case 10).—Inadequacy of fluid intake as a source of water for extracellular fluid space expansion. Slight negative fluid balance in a patient showing an 11-liter thiocyanate space expansion. The 11-liter expansion in this patient (Chart 5*B*) took place in the first 36 hours, during which his cumulative fluid balance was slightly negative.

‡ The water of metabolism of foodstuffs and that water released by metabolism of the patients' own fat cells have also been neglected in calculating the balances, creating a small error in the opposite direction.

§ The insensible losses in these patients are probably higher than those of patients undergoing similar operations without the preexisting peritonitis. Although postoperative sweat production is low, as has been shown by Hardy and Ravdin,[39] elevated metabolic rates in these patients presumably result in high respiratory losses.[33] These losses are considered further in the sixth paper.[34]

5. Weight Changes

All 24 of the patients were underweight. Their first weights after admission averaged 57.8 kg. (range, 45.5 to 69.1 kg.). In nine cases body weight was measured twice within the first 36 hours. Gains were recorded in four which did not exceed 1 kg. Four others showed no change in weight despite measured increases in thiocyanate volume, which in one case exceeded 9 liters. The ninth patient, whose thiocyanate space measured 15.3 liters on admission, lost 2 kg. during the 37-hour period in which his thiocyanate volume expanded to 23.8 liters. After 36 to 48 hours a universal trend of gradual weight loss took place, halting only after oral feeding was resumed.

6. Blood Pressure Changes

Despite fluid therapy, including, in 10 cases, transfusions of 400 to 500 cc. of whole blood, all 23 of the patients who came to operation exhibited operative or postoperative drops in systolic blood pressure averaging 30 mm. of mercury. The range was from 10 to 65 mm. of mercury; the biggest drop was recorded in a hypertensive patient (Case 17). The hypotensive period lasted from 2 to 12 hours, averaging 6½ hours.

INTERPRETATION

The measurements of the redistribution of fluid in the patient with a perforated ulcer point clearly to an immediate and rapid vascular dehydration and less clearly to an expansion of the interstitial compartment of the extracellular fluid space at the expense of cell water. Since an understanding of such fluid shifts is essential to an enlightened fluid therapy, a critical interpretation of the measurements is mandatory.

The observations pointing clearly to an immediate and rapid vascular dehydration are sixfold: 1. The plasma volumes were contracted. 2. The hematocrit values were high. 3. The serum protein concentrations were elevated. 4. The peripheral blood pressures were low. 5. The urinary volumes were scanty. 6. All of these changes were reversed by fluid therapy.

This vascular dehydration was what we expected in the ulcer patients. The chemical irritation of the peritoneum is like a burn. A wide surface is involved. Capillaries are damaged, causing an outpouring of fluid which flows through the tissue spaces and seeps into the peritoneal cavity, joining that which has come through the perforation. The protein concentration of this free fluid is comparable to that of the fluid oozing from a burn wound (4.6 gm./100 cc.). In both burns and perforated ulcers edema is formed by fluid from the plasma. The plasma volume is reduced and the hematocrit value elevated (Compare Charts 1*A* and 1*B*). More water than protein escapes into the interstitial spaces, with a resulting rise in the concentration of protein in the residual plasma.[8] Hypotension and diminished urinary output are common to both injuries, as plasma depletion reduces the effective blood volume.

It is possible that the fall in urinary excretion in these patients is due only in part to plasma loss with diminished glomerular filtration. The posterior lobe of the pituitary may also play a role in limiting urinary output.

The observations pointing to an expansion of the interstitial compartment with cellular dehydration are the measurements of the so-called extracellular space by the thiocyanate and sodium ions. The interpretation of these observations is open to doubt. Under normal conditions it is believed that the distribution of these ions is predominantly extracellular, only a small quantity penetrating the cells. The remainder diffuses in equal concentrations through the vascular and interstitial fluids. Expansions of the thiocyanate and sodium spaces ranged from 2 to 11 liters. Exogenous water as the source of this expansion is excluded by lack of both an appreciable weight gain and a sufficiently large fluid intake. Either water must have been withdrawn from cells or the anatomic extracellular space did not expand to the extent suggested by the two measurements. The passage of the ions into spaces not normally open to them, a more rapid

turnover rate between circulating and bone sodium, or chemical binding of the ions by protein could account for the reduced number of ions recovered 50 minutes after their injection.

If the thiocyanate and sodium ions measure the extracellular space, then the expanded space in these patients must represent edema. Those who deal with cutaneous burns see large quantities of edema beneath and around the wounds. In our study of burn patients expansions of the thiocyanate and sodium spaces were observed which were considered consistent with the volume of wound edema together with the edema fluid expressed or gravitating into the unburned areas.[38] In the ulcer patients, however, the expansions far surpassed clinical estimates of the volume of edema which might puddle beneath the peritoneal surfaces or flow through the tissue spaces and lymphatics to points remote from the site of perforation. Expansions of 2 or 4 liters might be compatible with the volume of edema which the surgeon sees in the upper abdomen at operation. Sodium expansions larger than 4 liters were encountered in 6 of the patients studied, and the thiocyanate expansions exceeded this range in 19 cases. In the third paper of this series,[31] objective evidence is given to support the clinical impression that the extracellular fluid volume did not expand by more than 3 or 4 liters. No rises in extracellular electrolyte concentrations occurred sufficient to produce the increase in osmotic pressure required to withdraw 4 liters of fluid from the cells.

A third argument against a large shift of intracellular water and in favor of the binding of thiocyanate and sodium ions by protein or their escape from the extracellular fluid is the disparity sometimes found in the volumes of the thiocyanate and sodium spaces. In normal persons the two spaces are almost identical. In 6 of the 10 ulcer patients in whom both spaces were measured there was also no significant difference between measurements, but in 4 others there were unexplained discrepancies. An 8 liter difference between the two spaces was encountered in Case 18 during the phase of his subdiaphragmatic abscess (Chart 6). Here, then, are two ions, formerly thought to measure the same anatomic space, giving widely different values.

Comparable discrepancies between the thiocyanate and sodium spaces have been found in two of our burn patients. In these, as in Case 18 (Chart 6) there was widespread inflammatory edema. It is hard to believe that the inflammatory barrier alone is responsible for the discrepancy, because in other burn patients with extensive inflamed

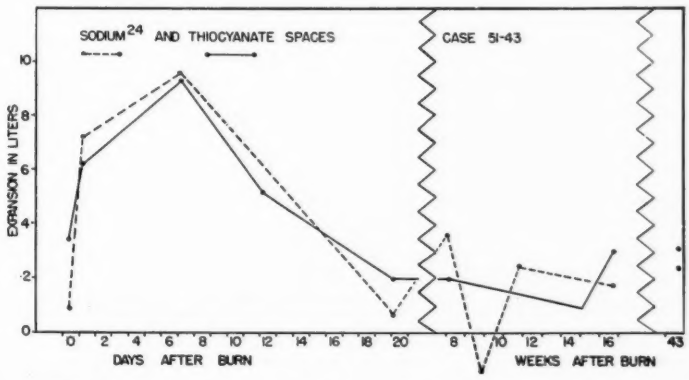

Chart 8.—Expansion of the extracellular fluid volume after a severe burn. The patient, a 30-year-old man who survived burns of 68% of his body surface (30% of third degree), showed expansion of the thiocyanate space comparable to that seen in the patient with a subdiaphragmatic abscess after ulcer perforation. Sepsis was rampant at the time of peak expansion. In this case there was no discrepancy between the thiocyanate and radioactive sodium volumes.

wounds no disparity was observed (Chart 8). The possibilities that there may be at times different distributions of the two ions outside the extracellular fluid or that one or both of them may be differently bound extravascularly offer the two most acceptable explanations.

The question of what the sodium and thiocyanate expansions mean is a practical one. If the extracellular space expands rapidly, a large quantity of fluid should be infused in the early hours to combat eventual cellular dehydration. If the expansion is only moderate and escape or trapping of the injected ions accounts for much of the increase in the thiocyanate and sodium volume, the giving of such an amount of fluid might be hazardous.

It has already been pointed out that a fuller interpretation of these fluid shifts must await consideration of the electrolyte data. Fluid shifts may also be influenced by colloids, which will also be discussed later. The plan for therapy emerging from these studies will be presented in the sixth paper, when all the evidence has been considered.[34]

SUMMARY AND CONCLUSIONS

Perforation of a peptic ulcer is followed by immediate and severe dehydration. The chemical insult to the peritoneum is followed by edema and loss in volume of the circulating plasma. Sixfold evidence of this vascular dehydration is presented.

The magnitude of the fluid losses of the ulcer patient is described.

Water is retained when fluid is given in therapy. Such therapy replenishes the plasma and abolishes the other evidences of dehydration.

The so-called extracellular fluid volume measured by the thiocyanate and sodium ions expands after perforation, reexpands with complications, and returns to normal with healing. The magnitude of the initial expansion exceeds clinical estimates of the volume of peritoneal edema. Several possible explanations are presented, and their implications with respect to fluid therapy are considered. Overenthusiastic fluid therapy is excluded as the source of the apparent extracellular fluid expansion.

Further consideration of the magnitude of cellular dehydration and the volume of fluid required by the perforated ulcer patient will be given in the subsequent papers.

REFERENCES

1. Cuthbertson, D. P.: Observations on the Disturbance of Metabolism Produced by Injury to the Limbs, Quart. J. Med. **1**:233, 1932.

2. Browne, J. S. L.: Conference on Bone and Wound Healing, Dec. 11 and 12, 1942, New York, Josiah Macy, Jr., Foundation.

3. Management of the Cocoanut Grove Burns at the Massachusetts General Hospital, Philadelphia, J. B. Lippincott Company, 1943.

4. Hirshfeld, J. W.; Williams, H. H.; Abbott, W. E.; Heller, C. G., and Pilling, M. A.: Significance of the Nitrogen Loss in the Exudate from Surface Burns, Surgery **15**:766, 1944.

5. Howard, J. E.: Protein Metabolism During Convalescence After Trauma: Recent Studies, Arch. Surg. **50**:166, 1945.

6. Randall, H. T.; Habif, D. V.; Lockwood, J. S., and Werner, S. C.: Potassium Deficiency in Surgical Patients, Surgery **26**:341, 1949.

7. Colebrook, L.: A New Approach to the Treatment of Burns and Scalds, London, Fine Technical Publications, 1950.

8. Moore, F. D.; Langohr, J. L.; Ingebretsen, M., and Cope, O.: The Role of Exudate Losses in the Protein and Electrolyte Imbalance of Burned Patients, Ann. Surg. **132**:1, 1950.

9. Ariel, I. M., and Kremen, J.: Compartmental Distribution of Sodium Chloride in Surgical Patients Pre- and Postoperatively, Ann. Surg. **132**:1009, 1950.

10. Elman, R.; Shatz, B. A.; Keating, R. E., and Weichselbaum, T. E.: Intracellular and Extracellular Potassium Deficits in Surgical Patients, Ann. Surg. **136**:111, 1952.

11. Johnson, H. T.; Conn, J. W.; Iob, V., and Coller, F. A.: Postoperative Salt Retention and Its Relation to Increased Adrenal Cortical Function, Ann. Surg. **132**:374, 1950.

12. Abbott, W. E.; Krieger, H.; Babb, L. I.; Levey, S., and Holden, W. D.: Metabolic Alterations in Surgical Patients: I. Effect of Altering the Electrolyte, Carbohydrate and Amino Acid Intake, Ann. Surg. **138**:434, 1953.

13. Collinson, H.: Some Present-Day Problems in the Surgery of Gastric and Duodenal Ulcer, J. A. M. A. **63**:1184, 1914.

14. Shawan, H. K.: Acute Perforated Ulcer, Am. J. Surg. **15**:277, 1932.

15. Blackford, J. M., and Baker, J. W.: Acute Perforating Peptic Ulcer: A Report of 21 Cases with Review of 933 Cases Reported by 13 Authors During the Last 10 Years, Am. J. Surg. **12**:18, 1931.

16. Eliason, E. L., and Ebeling, W. W.: Catastrophies of Peptic Ulcer, Am. J. Surg. **24**:63, 1934.

17. DeBakey, M., and Odom, C. B.: Significant Factors in the Prognosis and Mortality of Perforated Peptic Ulcer, South. Surgeon **9**:425, 1940.

18. Gerhardt, F.: Experience with Treatment of Perforating Gastric and Duodenal Ulcer at the First Surgical Clinic of the University of Vienna Between 1919 and 1933, Wien. klin. Wchnschr. **49**: 1389, 1936.

19. Graham, R. R.: The Surgeon's Responsibility in the Treatment of Duodenal Ulcer, Canad. M. A. J. **35**:263, 1936.

20. Tilton, B. T.: Low Mortality of Early Operation for Perforated Gastric and Duodenal Ulcer, Am. J. Surg. **32**:238, 1936.

21. Graham, R. R.: The Treatment of Perforated Duodenal Ulcers, Surg., Gynec. & Obst. **64**:235, 1937.

22. DeBakey, M.: Acute Perforated Gastroduodenal Ulceration, Surgery **8**:1028, 1940.

23. Strauss, A.: Primary Gastric Resection for Perforated Gastroduodenal Ulcers, Ann. Surg. **120**: 60, 1944.

24. Bedford-Turner, E. W.: Conservative Treatment of Duodenal Ulcer, Brit. M. J. **1**:457, 1945.

25. Perforated Peptic Ulcer Treated Without Operation, Letters to the Editor, Lancet **1**:467, 1947.

26. Glenn, F., and Harrison, C. S.: Acute Free Perforation of Peptic Ulcer: Complication of Ulcer Diathesis, A. M. A. Arch. Surg. **65**:795, 1952.

27. Mikal, S., and Morrison, W. R.: Acute Perforated Peptic Ulcer, New England J. Med. **247**: 119, 1952.

28. Schmitz, E. J.; Harkins, H. N.; Olson, H. H.; Moore, H. G., Jr., and Merendino, K. A.: Perforated Peptic Ulcer: A Study of 136 Cases in a County Hospital, Ann. Surg. **138**:689, 1953.

29. Burbank, C. B., and Roe, B. B.: Recent Experiences with Acute Perforation of Peptic Ulcers at the Massachusetts General Hospital: Review of 288 Cases, New England J. Med. **247**: 424, 1952.

30. Wight, A.; Hopkirk, J. F.; DeMuylder, E., and Cope, O.: Metabolic Derangements Imperiling the Perforated Ulcer Patient: II. Derangements and Shifts of Intracellular Electrolytes; The Need for Potassium, A. M. A. Arch. Surg., to be published.

31. Wight, A.; Taylor, S.; Minor, C. L.; Lohnes, W.; Hopkirk, J. F., and Cope, O.: Metabolic Derangements Imperiling the Perforated Ulcer Patient: III. Derangements and Shifts of Sodium and Chloride, A. M. A. Arch. Surg. to be published.

32. Wight, A.; Hopkirk, J. F., and Cope, O.: Metabolic Derangements Imperiling the Perforated Ulcer Patient: IV. Derangements of Nitrogen Metabolism and the Nitrogen Deficit, A. M. A. Arch. Surg., to be published.

33. Hopkirk, J. F.; Wight, A.; Merrington, W. R., and Cope, O.: Metabolic Derangements Imperiling the Perforated Ulcer Patient: V. Acceleration of Metabolic Rate and Altered Endocrine Activity, A. M. A. Arch. Surg., to be published.

34. Cope, O., and Wight, A.: Metabolic Derangements Imperiling the Perforated Ulcer Patient: VI. The Plan of Therapy, A. M. A. Arch. Surg., to be published.

35. Gibson, J. G., II, and Evelyn, K. A.: Clinical Studies of Blood Volume: Adaptation of Method to Photoelectric Microcolorimeter, J. Clin. Invest. **17**:153, 1938.

36. Crandall, L. A., Jr., and Anderson, M. X.: Estimation of State of Hydration of Body by Amount of Water Available for Solution of Sodium Thiocyanate, Am. J. Digest. Dis. & Nutrition **1**:126, 1934.

37. Kaltreider, N. L.; Meneely, G. R.; Allen, J. R., and Bale, W. F.: Determination of the Volume of the Extracellular Fluid of the Body with Radioactive Sodium, J. Exper. Med. **74**:568, 1941.

38. Cope, O., and Moore, F. D.: The Redistribution of Body Water and the Fluid Therapy of the Burned Patient, Ann. Surg. **126**:1010, 1947.

39. Hardy, J. D., and Ravdin, I. S.: Some Physiologic Aspects of Surgical Trauma, Ann. Surg. **136**:345, 1952.

Postmortem Skin Homografts in the Treatment of Extensive Burns

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The successful management of fluid-balance problems associated with the early phase in the clinical course of patients having extensive burns has prevented death from this complication in many of these patients. After survival through the early phase of the postburn period, these patients may develop further complications caused by the presence of a burn wound covering an extensive area. Such items as continued fluid loss, protein loss, and infection exact a great toll in the survival rate of these patients. Liedberg, Reiss, and Artz [1] have recently shown that septicemia is a common cause of death in the severely burned patient. This may result from a large open wound, colonized by many species of bacteria. These observations emphasize the need for early coverage of all burned areas.

In an ideal situation, burned areas should be grafted with sheets of autogenous skin, but in the extensively burned patient there may be insufficient donor sites. Such severely burned patients may be unable to tolerate the additional trauma of having skin removed. Application of skin homografts in these patients provides only a temporary coverage of the wound, but this procedure allows a period of time during which the patient's general condition may be improved, both from a nutritional standpoint and from that of local care of the wound. Furthermore, it makes practical the temporary coverage of some granulating areas while donor sites heal sufficiently to be used again. Homografts may be applied on the granulating areas without the need of general anesthesia. After the application of homografts, there is less infection, less fibrosis, and less discomfort. Usually the patient's morale improves and his nutritional intake is increased.

Application of postmortem homografts has been reported, but the procedure has not been used extensively.* Experiences of the Burn Study Section of the Surgical Research Unit demonstrate the repeated success of the application of postmortem homografts to granulating areas in patients having extensive burns. The benefit of homografting of burned areas with skin from a cadaver suggests that this procedure is a more practical method than homografts from living donors from the standpoint of morbidity and expense.

TECHNIQUE OF OBTAINING POSTMORTEM HOMOGRAFTS

As soon as possible after death, permission is obtained from the relatives to remove several strips of split-thickness skin from the body of the deceased person. Patients dying of cancer, tuberculosis, syphilis, septicemia, homologous serum hepatitis, other communicable diseases, or diseases having cutaneous manifestations are not suitable donors

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* References 2, 3, and 4.

of homografts. The body of the deceased person is brought to the operating room as soon as possible, and areas selected for removal of skin are treated with the usual preoperative skin preparation. The areas are draped, and sheets of skin from 0.012 to 0.015 in. in thickness are removed easily and rapidly with the Brown electric dermatome. The most accessible areas are the lower extremities and the back. After the skin is removed, it is placed on petrolatum-impregnated fine-mesh gauze with the cut surface of the skin away from the gauze. The skin and gauze are then folded in such a manner that the raw surfaces of the skin are in apposition. The skin is placed in a suitable covered container to which is added 1,000,000 units of penicillin and 1 gm. of streptomycin dissolved in 20 to 30 cc. of isotonic saline. The skin is then stored in the nonfreezing compartment of a refrigerator until it is needed. Successful takes have followed the use of postmortem skin which has been stored for as long as seven or even nine days.

Postmortem Homografts

Patient	Total Body Area Burned, %	Third-Degree Burn, %	Removal of Graft After Death, Hr.	Number of Homografting Procedures	Homograft Survival (Average Time)
1.....	60	45	4-6	9	3-4 wk.
2.....	60	50	3	1	3 wk.
3.....	70	47	6	1	47 days
4.....	50	25	6	1	26 days (died)
5.....	Unknown	40	7	3	2 wk.

RESULTS

During the past two years, several extensively burned patients have been treated with postmortem homografts. The five case reports that follow are typical and emphasize beneficial effects achieved by the use of homografts after extensive thermal injury. The Table outlines the pertinent data on these five cases concerning the size of the burn, the time of removal of skin after death of the donor, number of homografting procedures, and the average time of survival of the homograft.

Fig. 1.—This 10-year-old girl had 60% of her body surface burned, 45% of which was third-degree. On the 35th postburn day, the first group of postmortem homografts were applied to the back and buttocks. The photograph shows an 80% take of these homografts.

CASE 1.—A 10-year-old girl was burned when a playmate placed a burning newspaper under her dress. She sustained burns of the entire back, buttocks, thigh, groin, abdomen, and inner and anterior aspects of both arms. The total area of body surface burned was 60%, of which 45% was third degree. Thirty-one days after injury she was transferred to Brooke Army Hospital. All burned areas were granulating and were covered with dressings. Her general condition was fair; she had

Fig. 2.—The first group of homografts began to disintegrate 19 days after application. The two arrows point to large areas from which homografts have disintegrated. Additional homografts were placed on the denuded areas, and, as soon as the paitent's general condition improved, autografts were applied as the homografts disappeared.

bronchopneumonia, with temperature 103 F, and the hemoglobin was 13.3 gm.

Four days after admission, it was decided that coverage of the wound should be accomplished by homografting, because of the patient's septic course; the lack of available donor sites for autografting; the presence of bronchopneumonia, which made general anesthesia hazardous, and the loss of fluids and proteins from the burn surface. Postmortem homografts, taken four hours after death, were applied to both thighs and the anterior trunk, covering approximately 33% of the body surface. When dressings were changed four days later, there was evidence of an 80% take of the homografts (Fig. 1). Some areas in the lower abdomen and groin had not taken because of motion in these areas. Postmortem homografts which had been taken from a second body three and one-half hours after death and stored in a refrigerator for two hours were applied to the patient's back and buttocks without anesthesia on the 12th day after admission. When dressings were changed four days later, these homografts had taken, except for a small area on the right thigh. At this time, postmortem homografts from a third body were applied to the open areas on the lower abdomen and groin and also to the area on the right side. These homografts had been stored in the refrigerator for three days. Thus, on the 16th day after admission, all granulating areas had been covered with postmortem homografts from three different bodies. There was a 75% take of the third group of homografts.

The first group of homografts began to disintegrate 19 days after application (Fig. 2); the second set, after 21 days, and the third, after 24 days. As the homografts disappeared, postmortem homografts from other bodies were applied without anesthesia. Application of homografts totaled nine groups taken from nine different cadaver donors. The average survival time of homografts was between three and four weeks. The patient's general condition improved, but for several weeks she continued to have a fever (temperature from 102 to 104 F). Repeated blood cultures were negative.

Sheets of skin and small, postage-stamp autografts were applied six weeks after admission and periodically thereafter as the homografts disintegrated. This procedure was repeated many times; the patient was completely covered with autografts 140 days after injury (Fig. 3).

Case 2.—A 5-year-old American boy was burned in France as the result of an explosion of a jet plane which crashed in the yard of his home. He was given initial care in various United States Army Hospitals in Europe prior to evacuation to the United States. He arrived at Brooke Army Hospital 16 days after sustaining extensive burns.

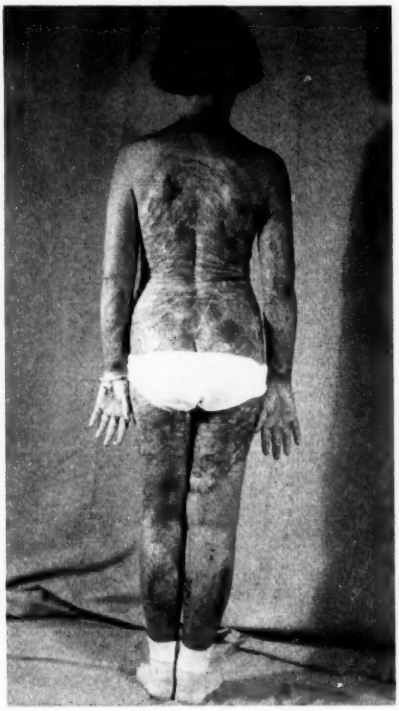


Fig. 3.—Autografts 140 days after injury. This photograph was taken at the time of discharge from the hospital.

There were burns of the right side of the face, back of the head, neck, right arm, back, and both lower extremities. It was estimated that 10% of his body was covered with partial-thickness burns and 50% with full-thickness burns.

On admission, his temperature fluctuated between 102 and 103 F, and his hemoglobin was 11.3 gm. Eight days after admission, homografts that had been taken from a cadaver three hours after death and stored in a refrigerator for three days were applied to the legs and back. There was a 90% take of these homografts, and they survived for 21 days. The patient's face, arms, and neck were covered with available autografts. Excessive skin from three other burned patients was available for further homografting procedures. As more donor sites became available, postage-stamp autografts were used to cover areas from which the homografts had disintegrated. Complete skin coverage by autografts was achieved 91 days after this patient was burned.

Case 3.—A 22-year-old soldier sustained extensive burns when a shell exploded in the magazine of a self-propelled howitzer. He was admitted to

Fig. 4.—This soldier had sustained burns of 70% of the body surface, of which 47% was third-degree. He experienced a massive gastrointestinal hemorrhage, presumably from a Curling's ulcer, and septicemia developed. Owing to his critical condition, postmortem homografts were applied to both lower extremities on the 33d postburn day. There was an unusually good take of the homografts, and this photograph was taken 11 days after application. These homografts survived for 47 days.

Brooke Army Hospital seven days after injury. There were third-degree burns over both arms and both lower extremities and deep dermal burns of the face, anterior trunk, and part of the back. Burns covered 70% of the body surface, with an estimated 47% of third-degree burns. Autografts were applied to the arms under general anesthesia on the morning of the 24th postburn day. That evening he experienced a massive gastrointestinal hemorrhage, presumably from a Curling's ulcer, and 3500 cc. of blood was required in the first 24 hours. The bleeding subsided after conservative therapy.

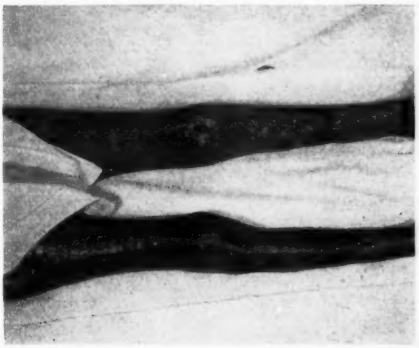
Because of the lack of further donor areas and the presence of septicemia due to a hemolytic Staphylococcus aureus in a critically ill patient, postmortem homografts were applied to both lower extremities on the 33d postburn day. The skin applied had been obtained six hours after death and had been stored in the refrigerator for 12 hours prior to application. There was 100% take of the homografts, and they remained intact for 47 days (Fig. 4). Postage-stamp autografts taken under local anesthesia were applied as the homografts disappeared. Complete coverage by autografts was achieved on the 105th postburn day.[5]

Case 4.—A 20-year-old soldier was burned extensively in the same accident as the preceding patient. He was admitted to Brooke Army Hospital seven days after injury. There were third-degree burns of the chest and both lower extremities. There were deep dermal burns on the arms and anterior trunk. The extent of burn was 50% of the body surface, including 25% third-degree burn. On the 27th postburn day, both lower extremities were covered with postage-stamp autografts. The patient developed septicemia due to a hemolytic S. aureus on the 28th postburn day. On the 34th day after the burn, postmortem homografts were applied to the right chest. These homografts had been removed from a donor body six hours after death and had been kept in a refrigerator for 48 hours. They were applied on the ward without anesthesia, and no dressings were used. There was a 100% take of the grafts, and they remained firmly attached until the patient's death, 28 days later. Death was caused by septicemia due to a hemolytic S. aureus, which was resistant to all antibiotics.

Case 5.—A 20-year-old soldier was burned in Korea when he was cleaning a small generator with gasoline. He received initial treatment at a mobile Army surgical hospital, and seven days later he was transferred to Tokyo Army Hospital. He had deep burns of both lower extremities, both hands, genitalia, buttocks, and some additional partial-thickness burns. Third-degree burns involved 40% of the body surface. While the patient was at Tokyo Army Hospital, split-thickness autografts were taken from his anterior and posterior trunk and applied to both lower extremities. When he was evacuated, 53 days after injury, from 80% to 90% of the burned areas were covered with autogenous grafts, but his donor sites had not yet healed.

After several days in transport, he arrived at Brooke Army Hospital with all the donor sites severely infected and converted to full-thickness skin loss. Many of the recently grafted areas had become infected. He began to lose weight rapidly. Six months after injury he weighed 81 lb., and 35% of his body surface was still granulating donor areas. Further attempts at autografting resulted in

Fig. 5.—As the homografts disappeared, small postage-stamp autografts taken under local anesthesia were applied. Complete coverage by autografts was achieved on the 105th postburn day. This photograph was taken after complete healing had occurred.



poor wound healing, infection, and conversion of the donor sites to full-thickness injury. Homografts taken from a donor body four hours after death were applied to all open wounds. The homografts began to disintegrate in about two weeks but the patient was beginning to gain weight. As the homografts disappeared, postmortem homografts were applied from two other donor bodies. The patient improved considerably, and eventually postage-stamp autografts were used to cover the areas as the homografts disappeared. He continued to gain weight and was discharged in good condition.

For many years, it has been a recognized fact that the cardinal principles in the management of a patient with extensive burns are vigorous supportive therapy and early closure of wounds. When large areas require grafting donor skin may not be available. In other patients, who have become severely debilitated following a prolonged period with open wounds, further removal of the patient's skin may be contraindicated. In such instances, the procedure of applying a homograft has become well established. By temporary closure of the wound, homografts prevent infection and further deterioration of the patient by conservation of fluid, electrolyte, and protein losses.

In a recent study on clinical homografts in burns, Jackson [5] reports that although it is not difficult to secure donors frequently they are inconvenienced because of the necessity of admission to the hospital. When skin was taken from the leg, thigh, and buttocks of one donor, he was hospitalized for 10 days and was forced to be away from work for a week after he returned home.[5] Sanders and Moore removed 19 sheets of skin from 18 donors, and the donors were able to remain ambulatory. But the difficulty, inconvenience, and morbidity associated with the removal of skin from live donors are a deterrent to the use of homografts in burns.[6] Postmortem homografts eliminate all these disadvantages and make available an unlimited source of large sheets of skin. These sheets of skin may be applied to the granulating areas without the need of general anesthesia, and thus additional injury to the patient is avoided.

The efficacy of postmortem homografts, as demonstrated at the Surgical Research Unit in the past two years, indicates that this procedure is extremely practical. It is usually easier to obtain consent for the removal of postmortem grafts than it is to obtain consent for an autopsy. If relatives of the deceased person are made to understand the need for skin, frequently they welcome an opportunity to assist in saving the life of an extensively burned patient. It would appear that the public needs to be educated on this subject, in order to emphasize the value of cadaver homografts. Additional publicity concerning the value of this procedure would help nonprofessional people realize the need and advantages of postmortem homografts. When the public realizes the lifesaving character of these homografts, little difficulty will be encountered in obtaining permission to take skin from donor bodies.

Postmortem homografts should be used more extensively. As yet it is not known how long homografts may be stored successfully or how long skin remains viable after death. Further knowledge of the problems related to the time interval after death in which skin may be removed and methods and length of storage prior to application must be obtained in order to understand more fully the feasibility of using postmortem homografts.

SUMMARY

Although homografts provide only a temporary coverage for the wound, they may be lifesaving in extensively burned patients. Their application allows a period of time during which the general condition of the patient may be improved, and they prevent invasive infection.

The use of skin from a cadaver is much more practical than homografts from living donors. Clinical experience with postmortem homografts during the past two years has demonstrated the success of these grafts in extensively burned patients. Typical case histories of five patients are recorded.

Grafts were removed from donor bodies from three to seven hours after death. They survived from 2 weeks to 47 days.

The use of postmortem homografts provides an easy, practical method of achieving temporary wound closure in extensively burned patients.

REFERENCES

1. Liedberg, N. C. F.; Reiss, E., and Artz, C. P.: Infection in Burns: III. Septicemia, a Common Cause of Death, Surg., Gynec. & Obst. **99**:151 (Aug.) 1954.

2. Dogo, G.: Survival and Utilization of Cadaver Skin, Plast. & Reconstruct. Surg. **10**:10 (July) 1952.

3. Brown, B.; Fryer, M. P.; Randall, P., and Lu, M.: Postmortem Homografts as Biologic Dressings for Extensive Burns and Denuded Areas, Ann. Surg. **138**:618 (Oct.) 1953.

4. Brown, J. B., and Fryer, M. P.: Postmortem Homografts to Reduce Mortality in Extensive Burns, J. A. M. A. **156**:1163 (Nov. 20) 1954.

5. Jackson, D.: Clinical Study of the Use of Skin Homografts for Burns, Brit. J. Plast. Surg. **7**:26 (April) 1954.

6. Sanders, G. B., and Moore, R. H., Jr.: Use of Homografts in Extensively Burned Patients, Am. J. Surg. **80**:637 (Nov. 15) 1950.

Primary Mesenteric Venous Thrombosis

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Thrombosis within mesenteric veins is often associated with other primary abdominal pathology, such as suppurative disease, volvulus, strangulated hernia, congestive splenomegalia, neoplastic disease, cirrhosis of the liver, and trauma.* Mesenteric venous thrombosis which appears to be primary and without known cause, while less frequent, also occurs. In a postmortem study of 99 patients with mesenteric venous occlusion due to thrombosis by Johnson and Baggenstoss,[1] there were 8 cases in which no etiologic factor was evident, but these cases were not discussed in detail. In 1950, Berry and Bougas [2] presented 13 instances of primary mesenteric venous thrombosis in 12 patients with 4 survivals, 1 with two episodes. The latter article is distinctive in that mesenteric venous thrombosis is discussed in pure form, which adds emphasis to Warren and Eberhard's [3] suggestion that mesenteric venous thrombosis is a distinct entity separate from mesenteric arterial thrombosis.

There has developed a large literature dealing with mesenteric vascular occlusion, but usually the authors fail to differentiate between primary venous and primary arterial mesenteric thrombosis or emboli, and not infrequently they state that the two cannot be differentiated.† In 1953, Mersheimer and others,[6] after an exhaustive review of the literature, found 212 successful bowel resections for mesenteric vascular occlusion and added 5 cases. There is no way to know how many of these 212 patients had primary venous, secondary venous, or arterial thrombosis or emboli, for, as stated, these cases are usually lumped together under the title mesenteric vascular occlusion. Of the 5 patients who survived and were added by Mersheimer and co-workers,[6] it is evident from the case presentation and the authors' statement that 4 of these were cases of venous thrombosis, and I believe that of the 212 the greater percentage are of either the primary or secondary venous variety rather than the arterial. Mesenteric arterial thrombosis or embolism is a catastrophic abdominal emergency, as a rule, with sudden severe onset and high mortality, as contrasted to the less dramatic onset of mesenteric venous thrombosis.[7]

By the presentation of two of my patients who have had three attacks of primary mesenteric venous thrombosis and one patient that Dr. R. S. Sparkman has permitted me to report on, I wish to add further emphasis to the fact that primary mesenteric venous thrombosis does occur, that it does not usually present itself clinically as a catastrophic abdominal emergency but is insidious in onset and slowly progressive, and that the prognosis is favorable after surgical excision of the involved segment and administration of anticoagulants.

REPORT OF CASES

CASE 1.—A man aged 31, was admitted to the Medical Arts Hospital in June, 1948. He stated that, except for malaria while in the armed service (1945), he had never been ill until four days prior to admission. At that time he developed vague mild abdominal discomfort and slight nausea, but with no vomiting. The following day, mild cramping abdominal pain was present; in the late afternoon there were two liquid bowel movements, but no gross blood was seen. The following day, the third day of his illness, the pain, while not severe, became

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* References 1 and 2.

† References 4 and 5.

constant and was diffuse across his upper abdomen. During the night he vomited twice. The vomitus consisted of gastric contents only. By the morning of the fourth day of his illness, the pain was so severe across the upper abdomen that he was given ⅙ grain (10 mg.) of morphine, with relief. At the time of his admission to the hospital, he complained of moderately severe, constant pain across the upper half of his abdomen.

The patient did not appear acutely ill. His temperature was 100 F. The chest was clear. The heart was normal. Examination revealed diffuse tenderness, Grade 1, over the entire upper half of the abdomen. The liver, kidneys, and spleen were normal to palpation. No masses could be palpated. No hernia was present. There was no evidence of peritoneal irritation. Examination of the rectum was negative.

An AP x-ray film of the abdomen was negative for free air, but there was a little gas in two loops of small bowel. The white blood cell count was 21,000, with 80% polymorphonuclear cells present.

Through the afternoon and evening the patient was examined on several occasions, but a definite diagnosis was not evident.

The following morning, the fifth day of the patient's illness, he complained of severe pain across the entire upper abdomen. There was nausea, and he had vomited twice during the early morning. There was no gross blood in the vomitus.

The abdomen was moderately distended, and there was marked tenderness with muscle spasm across the entire upper half, particularly in the left upper quadrant. No masses could be palpated.

The temperature was 100 F. The white blood cell count was 24,000, with 93% polymorphonuclear cells present.

Operation.—An abdominal exploration was done. A large quantity of serosanguineous fluid was present in the peritoneal cavity. There was mesenteric venous thrombosis involving the upper 2 ft. of jejunum. This was resected, and gastrointestinal continuity was reestablished by means of an end-to-end jejunojejunostomy.

Pathology.—"The specimen consists of 64 cm. of small intestine and attached mesentery. The bowel, particularly the central two-thirds, is deep purple-black, markedly thickened, and indurated. The lumen of this portion of the bowel contains blood clots. The bowel wall is thickened up to 1.5 cm. and is grossly hemorrhagic. The mucosa is very edematous, and there appears to be some ulceration in places. The mesentery is friable, very thickened, and grossly hemorrhagic. On section of the mesentery the veins were seen to contain well-organized blood clots."

Microscopic Findings.—"Cross section of the bowel wall shows the wall to be markedly thickened. The normal architecture is lost, and there is diffuse infiltration of blood cells. The mucous membrane is seen to be ulcerated in some of the sections. Sections of the mesentery reveal edema, congestion, and some inflammatory infiltration around the veins. There is thrombosis of the mesenteric veins. The thrombi show some lamination and are attached to the endothelium at focal points. The arteries appear normal."

Pathological Diagnosis.—"Jejunum: venous mesenteric thrombosis with hemorrhagic infarction of jejunum" (Dr. Marvin D. Bell, pathologist).

CASE 2 and 2*A*.—A woman, aged 50, was admitted to Baylor Hospital on May 16, 1951. The patient was stated to be addicted to phenobarbital and complained of mild, vague, slightly cramping, generalized abdominal pain of three days' duration. There had been recurring transient nausea, and the patient had vomited once in the afternoon prior to admission. The vomitus did not contain gross blood. The past history was noncontributory except that in 1941 she had had bilateral thrombophlebitis in the deep veins of her legs.

The patient did not appear acutely ill. The temperature was 99 F. The pulse rate was 88, and the respiratory rate was 20. The lungs were clear. The heart was normal. The abdomen was slightly distended. No masses could be palpated. No hernia was present. There was some diffuse tenderness over the abdomen, but there was no localization and no muscle-guarding. Peristalsis could be heard but was faint. Examination of the pelvis and rectum was negative.

The white blood cell count was 14,900, with 83% polymorphonuclear cells present. An AP x-ray film of the abdomen was reported as normal.

In the late afternoon following her admission, the fourth day of her illness, she became nauseated and vomited twice. There was no gross blood in the vomitus. The generalized pain was still present and was just as vague. No peristalsis could be heard. The abdomen was more distended than it had been earlier in the day, and there was a suggestion of localization of pain, with muscle-guarding in the right lower quadrant.

The white blood cell count was now 20,000, with 91% polymorphonuclear cells present.

A diagnosis of appendicitis was made.

Operation.—On my opening the abdomen through a McBurney incision, there was a gush of serosanguineous fluid. The appendix was normal. The incision was enlarged to admit my hand, and in the left upper quadrant of the abdomen a loop of thickened bowel was palpated. The incision was closed, and a left midrectus incision was made. A 2 ft. segment of jejunum was involved in mesenteric venous thrombosis. The involved segment was re-

sected, and an end-to-end jejunojejunostomy was done.

Pathology.—"The specimen consists of a 50 cm. segment of small bowel. In the center of the resected bowel there is a segment measuring roughly 20 cm. that has a dark reddish-blue color with areas of subserosal hemorrhage. This section is markedly thickened and indurated. On either end of this segment the bowel is discolored and edematous, gradually fading into normal intestine. The mesentery attached to the bowel is hemorrhagic, moderately thickened, and indurated. On cross sectioning the mesentery the veins are found to contain blood clots. The arteries appear normal. The open bowel shows the entire wall to be thickened and hemorrhagic, measuring up to 1.5 cm. in thickness. The mucosa is markedly edematous throughout the entire extent of the specimen."

Microscopic Findings.—"Cross section of the above-described bowel reveals the lining mucosa to be necrotic. The wall is markedly thickened, and the normal architecture is lost. It is markedly edematous and congested with interstitial hemorrhage. Sections of the mesentery reveal edema, congestion, and inflammatory infiltration about the veins and in the fibrofatty tissue. Thrombosis of the mesenteric veins is evident. The thrombi show some laminations and are definitely attached to the endothelium at focal points. The arteries appear normal."

Pathological Diagnosis.—"Mesenteric venous thrombosis with gangrene of segment of small bowel" (Dr. J. M. Hill, pathologist).

Postoperative Course.—Twelve hours after surgery the patient was given 50 mg. of heparin intravenously, followed by 100 mg. of heparin every four hours. Coagulation time was followed with the Lee-White test and was maintained at between 15 and 30 minutes. On the sixth postoperative day administration of bishydroxycoumarin (Dicumarol) was begun orally, and the prothrombin time was reduced and maintained at between 25% and 35% of normal.

Convalescence was uneventful, and the patient was discharged on the 14th postoperative day with instructions to take bishydroxycoumarin each day.

Five days later the patient was readmitted to Baylor Hospital. She stated that she had not taken any of the bishydroxycoumarin as ordered and complained of generalized abdominal pain of a severe cramping character. There was nausea, and she had vomited once. The vomitus contained gastric contents only. There had not been a bowel movement in 48 hours.

The temperature was 99.6 F. The abdomen was moderately distended. There was diffuse tenderness but no rigidity. Hyperactive peristalsis was present.

An AP x-ray examination of the abdomen showed several loops of grossly distended small bowel containing gas. The white blood cell count was 19,000, with 91% polymorphonuclear cells present. The prothrombin time was 100% of normal. The Lee-White coagulation time was 7 minutes.

Second Operation.—The abdomen was explored through a right midrectus incision. There was a large quantity of serosanguineous fluid within the peritoneal cavity. A 14 in. segment of midileum was involved with mesenteric venous thrombosis. The involved segment was resected, and a side-to-side ileoileostomy was done. The small bowel proximal to the area of thrombosis was greatly distended. The intestine at the site of the recent resection appeared normal.

Pathology.—"The specimen consists of a segment of small intestine measuring approximately 50 cm. in length. In the center of the resected bowel there is a segment 22 cm. in length in which the serosal surface is markedly discolored and deep reddish-black. This segment is greatly thickened, indurated, and edematous. The attached mesentery is likewise hemorrhagic and thickened. The open bowel contains blood clots in its lumen, and the bowel wall in the previously described blackish area appears to be almost completely replaced by hemorrhage."

Microscopic Findings.—"The architecture of the bowel wall is completely destroyed, and the wall is infiltrated with hemorrhage. The mucosa is destroyed in some areas. The section of mesentery is markedly edematous and hemorrhagic. The veins contain laminated thrombi attached to the walls. The arteries are congested but appear normal."

Pathological Diagnosis.—"Mesenteric venous thrombosis with hemorrhagic infarct of the small bowel" (Dr. J. M. Hill, pathologist).

Postoperative Course.—Eight hours postoperatively the patient was given heparin intravenously followed by regular doses given intramuscularly, such that the Lee-White coagulation time was maintained at between 15 and 25 minutes. On the sixth postoperative day bishydroxycoumarin therapy was begun orally, and the prothrombin time was reduced to between 25% and 35% of normal.

The patient made an uneventful convalescence and was discharged from the hospital on the 15th postoperative day. Since that time she has been maintained on a daily dosage of bishydroxycoumarin and has been followed with weekly determinations of prothrombin time; the prothrombin time has been maintained at 35% or 40% of normal.

The patient has remained well except that she has been readmitted to the hospital four times because of self-induced acute barbiturate intoxication. On two of these admissions she also had a thrombosis of a superficial vein across her right thigh.

CASE 3.—A woman, aged 40 (patient of Dr. R. S. Sparkman), was admitted to Baylor Hospital Aug. 14, 1954. The patient stated that she was perfectly well until one week prior to admission, when she began to feel general malaise with loss of appetite. Within the next 24 hours there developed generalized abdominal pain, which persisted. The pain was not intense until one day prior to admission, when it became severe, constant, and cramp-like. During periods of intense pain there had been associated nausea and vomiting. No blood was noted in the vomitus. The past history was negative except for a history of thrombophlebitis in the right leg.

The patient appeared to be in great distress with diffuse abdominal pain. The temperature was normal. The pulse rate was 90. The blood pressure was 140/90. The abdomen was obese and rotund. The abdomen was tender generally, but the tenderness was marked in the right lower quadrant. Rebound tenderness was present. No masses could be palpated. Peristalsis could be heard but was diminished. The pelvic and rectal examinations were negative.

The white blood cell count was 20,600, with 94% polymorphonuclear cells present.

A diagnosis of acute appendicitis was made.

Operation.—The abdomen was opened through a McBurney incision. There was a large quantity of serosanguineous fluid within the peritoneal cavity. The appendix was normal. A segment of ileum 1 ft. in length, approximately 2 ft. above the ileocecal valve, was involved in mesenteric venous thrombosis. The involved segment was resected, and an end-to-end ileoileostomy was done.

Pathology.—"The specimen consists of a segment of small bowel and attached mesentery 30 cm. in length. The central portion of the segment is deep dusky purple. The bowel in the middle part of the specimen is 1.5 cm. in thickness, while at each end it is 2 mm. in thickness. The wall of the bowel is of usual consistency at the lateral margins of the specimen, but the central portion is red and hemorrhagic. The attached mesentery is markedly thickened and hemorrhagic. The mucosa is edematous throughout and markedly hemorrhagic in the central portion of the specimen, but there is no gross necrosis."

Microscopic Findings.—"In the sections taken from the central portion of the specimen, the architecture of the bowel wall is completely destroyed and the wall is diffusely infiltrated with hemorrhage. The mucosa is markedly hemorrhagic and ulcerated in focal areas. The sections taken from the mesentery are markedly edematous and hemorrhagic. The veins contain laminated thrombi. The arteries are engorged but appear normal."

Pathological Diagnosis.—"Ileum: mesenteric venous thrombosis, with hemorrhagic infarct of ileum" (Dr. J. M. Hill, pathologist).

Postoperative Course.—During the five days subsequent to surgery the clinical course was one of steady decline, punctuated by episodes of hypotension and collapse. The patient complained of severe abdominal pain. The abdomen became increasingly distended, with evidence of peritoneal irritation. The patient died on the fifth postoperative day.

During the postoperative period continuous gastric suction was maintained, and in the 24 hours prior to the patient's death gross blood was noted in the drainage. There had been no passage of gas by rectum at any time. The patient did not receive anticoagulants.

Necropsy.—"Examination of the abdominal cavity revealed generalized peritonitis secondary to gangrenous infarction of approximately 165 cm. of ileum and jejunum. The area of infarcted small bowel began at the previous suture line, which was intact and extended proximally. The distal 40 cm. of ileum appeared normal. The involved bowel was deep purple-black, and the wall was markedly thickened and indurated, as was the corresponding mesentery. Within the lumen of this infarcted portion of bowel the contents were seen to be liquid and black. The arcuate veins of the lower portion of the superior mesenteric vein were blocked by dense adherent thrombi. The main trunk of the superior mesenteric vein was not thrombosed."

Pathological Diagnosis.—"1. Small bowel: (*a*) strangulation necrosis of ileum and jejunum (approximately 165 cm.); (*b*) thrombosis of the superior mesenteric vein; 2. Peritoneum: acute peritonitis; 3. Lung: (*a*) atelectasis, focal; (*b*) pleuritis, subacute and focal; 4. Liver: fatty metamorphosis; 5. Thyroid: chronic thyroiditis; 6. Postoperative status: resection of 30 cm. of terminal ileum; end-to-end anastomosis, intact; 7. Adrenal cortex: lipoid depletion" (Dr. J. M. Hill, pathologist).

COMMENT

Pathology.—The pathology was identical in each instance. There was considerable blood-tinged serous fluid in the peritoneal cavity. The involved mesenteries were markedly thickened, indurated, and hemorrhagic. The corresponding segments of bowel were also markedly thickened, indurated, and hemorrhagic. In color the intestines and mesenteries were brick-red to deep purple-black. The maximal thickening and discoloration of

the mesenteries occurred near the bowel and gradually diminished toward the root of the mesentery, indicating that the process of thrombosis began in the periphery. This was very evident on necropsy in Case 3, in which the arcuate veins were grossly thrombosed and the main trunk of the superior mesenteric vein was normal. Looking at the involved segments of bowel, one could see that the disease was spreading proximally and distally in the mesenteries, as the maximum involvement was in the middle of the diseased segments.

The microscopic picture was likewise identical in each instance. The sections of bowel wall showed strangulation necrosis. There was marked hemorrhagic infiltration of the entire wall, and the mucosa was disintegrating. A thin layer of fibrin which enmeshed many polymorphonuclear cells could be seen on the serosa. Sections taken from the mesenteries showed fatty tissue with focal hemorrhagic areas and some inflammatory cell infiltration. In all sections thrombosis was evident in the veins. The thrombi were adherent to the vein walls, and platelet ridges were prominent. There were many polymorphonuclear cells surrounding the thrombosed vessel walls. The arteries were congested, but no thrombi were present.

General Observations.—In two of the cases (Cases 2 and 3) there was an antecedent history of thrombophlebitis of the lower extremities, and in one case (Case 2) minor superficial phlebitis of a leg occurred two and three years postoperatively. North and Wollenman [8] called attention to apparent primary mesenteric venous thrombosis occurring in a course of migratory thrombophlebitis. Further, these authors emphasized the insidious onset of mesenteric venous thrombosis and stressed the important implication of antecedent thrombophlebitis in a patient presenting puzzling undiagnosed abdominal pain.

Case 2 is unusual in that a second attack of mesenteric venous thrombosis which involved an entirely separate segment of small bowel occurred within three weeks of the primary attack and was successfully treated by resection and anticoagulants. One of Berry and Bougas' [2] patients (Case 1 and 1*A*) had a recurrence of mesenteric venous thrombosis three years following the primary attack and was treated successfully. Strohl and Lasner [9] reported on a patient who survived two attacks of mesenteric venous thrombosis 40 days apart.

It is apparent from the autopsy in Case 3 that a recurrence did not take place but that the cause of death was a continuation of the primary attack. This occurred in spite of the fact that at the time of the primary surgery the diseased segment was well demarcated.

SUMMARY

Three patients who had had four attacks of primary mesenteric venous thrombosis are presented. Two of the patients survived three attacks, and one died.

In each instance the onset was gradual, with vague abdominal pain which gradually increased in severity. In the two instances in which the ileum was involved, the pain was cramping in character and hyperactive peristalsis was present, presenting a picture of small bowel obstruction. In each of the four attacks the patient's temperature did not exceed 100 F, and the white blood cell count was increased to above 20,000, with a marked increase in polymorphonuclear cells. Shock was not present in any instance.

In each of the primary attacks the patients were operated upon the fifth, fourth, and fifth day, respectively, indicating clearly that this disease does not present itself clinically as an acute surgical emergency.

The prognosis of primary mesenteric venous thrombosis is favorable after resection of the involved intestine and administration of anticoagulant therapy.

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REFERENCES

1. Johnson, C. C., and Baggenstoss, A. H.: Mesenteric Vascular Occlusion: I. Study of 99 Cases of Occlusion of Veins, Proc. Staff Meet., Mayo Clin. **24**:628-636, 1949.

2. Berry, F. B., and Bougas, J. A.: Agnovenic Venous Mesenteric Thrombosis, Ann. Surg. **132:** 450-474, 1950.

3. Warren, S., and Eberhard, T. P.: Mesenteric Venous Thrombosis, Surg., Gynec. & Obst. **61:** 102-121, 1935.

4. Musgrove, J. E., and Seybold, W. D.: Symposium on Abdominal Surgery: Mesenteric Vascular Occlusion, S. Clin. North America **30:** 1063-1071, 1950.

5. Morris, W. R.: Mesenteric Vascular Occlusion, M. Ann. District of Columbia **24:**12-16, 1955.

6. Mersheimer, W. L.; Winfield, J. M., and Fankhauser, R. L.: Mesenteric Vascular Occlusion, A. M. A. Arch. Surg. **66:**752-768, 1953.

7. Whittaker, L. D., and Pemberton, J. deJ.: Mesenteric Vascular Occlusion, J. A. M. A. **111:** 21-24, 1938.

8. North, J. P., and Wollenman, O. J., Jr.: Venous Mesenteric Occlusion in the Course of Migrating Thrombophlebitis, Surg., Gynec. & Obst. **95:**665-671, 1952.

9. Strohl, E. L., and Lasner, J.: Mesenteric Vascular Occlusion, A. M. A. Arch. Surg. **60:**339-342, 1950.

Silicone Rubber as Aortic Grafting Material

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The introduction of Vinyon-N cloth by Voorhees, Jaretzki, and Blakemore in 1952 opened a new era in vascular grafting.[1] A follow-up study by the same group [2] reported 18 clinical cases of arteriosclerotic aneurysm resection, with replacement by Vinyon-N cloth. The material is easy to suture, strong, readily obtainable, and relatively inexpensive. Grafts fashioned from Vinyon-N cloth maintain a patency comparable with that of aortic homografts. Other plastic cloths, such as Dacron, nylon, and Orlon,[3] have been used recently, with considerable success. Much research is being done at many centers in an effort to determine the best plastic cloth and the most favorable method of application.

Despite these enthusiastic reports, there are certain inherent disadvantages of all such plastic cloths being used for vascular grafts at present. None is truly elastic, and the ultimate fate of all is to become incased in a fibrous restraining capsule. Although even completely rigid prostheses will function in the aorta,[4] it is unlikely that such grafts would be acceptable in the smaller arteries, such as the carotid and femoral. The elasticity of blood vessels is of vital importance in maintaining the diastolic pressure, and, in many cases requiring vascular grafts, this factor may be significant. The insertion of a rigid or ultimately rigid graft may result in damaging diastolic pressure reduction in the patient with cerebral arteriosclerosis or peripheral vasospasm. It is for this reason that we have tested an elastic material, silicone rubber, for aortic grafting. Natural rubber has been tried in aortic grafting,[5] but early thrombosis resulted.

Silicone rubber is a dimethyl siloxane polymer and possesses the interesting properties of other silicone compounds. These substances withstand extremes of temperature, are acid- and alkali-resistant, and can be produced in various physical states.[6] They have been shown to be relatively inert in the tissues [7] and to possess extreme water repellency. Until recently, silicone rubber was of very limited usefulness owing to its low durability and tensile strength. An improved and much stronger silicone rubber product is now available and has been used in this study.

METHODS

Adult mongrel dogs ranging in weight from 10 to 20 kg. were used for all experiments, and intravenous pentobarbital (Nembutal) was the anesthetic. Penicillin, 300,000 units intramuscularly, was given on the first postoperative day. A midline incision extending from the xiphoid to a point midway between the pubis and the umbilicus was made, and the abdominal aorta above the inferior mesenteric artery was mobilized. Crocodile clips * were applied, and a 2.5-cm. segment of the aorta was resected just above the inferior mesenteric artery. Silicone rubber tubes † 4 cm. long were folded back at

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† Obtained from the Connecticut Hard Rubber Co., New Haven, Conn.

each end so that the prosthesis was 3 cm. long; afterward they were sutured in the aortic defects by either continuous whipping or everting anastomosis with 00000 nonabsorbable surgical (silk) sutures. The silicone rubber used in this study was 0.5 mm. thick and translucent and had high tensile and tear strength; when the edges were folded back, the material took sutures without a tendency to tear. When the crocodile clips were removed, there was very slight bleeding from the suture line which ceased almost immediately. Blood could be seen swirling in the grafted segment, and excellent pulsations were felt and observed. The graft could be seen to widen with each heartbeat and to return to resting diameter during diastole. Good approximation of graft to host aorta size was obtained in all cases. Aortograms were performed in some experiments with the use of 10 cc. of 35% acetrizoate (Urokon) solution injected retrogradely into the femoral artery. Follow-up periods ranged from 1 to 46 days, and femoral pulses were taken every few days as a crude method of ascertaining graft patency.

RESULTS

The results of 10 dog experiments with silicone rubber aortic grafts are summarized in the Table. In eight animals, the grafts were solidly thrombosed one week after operation. In the two cases with patent grafts at necropsy, no diminution of elastic expansion and contraction was noted as compared with that at time of insertion. Although there was a thin fibrous capsule around the silicone rubber grafts in all instances, evidence of local tissue reaction was minimal. This is in contrast to the much greater local fibrosis and tissue reaction around such plastics as Orlon.‡

COMMENT

Under the conditions of this study, silicone rubber tubes used as aortic grafts exhibited a prohibitive incidence of thrombosis. Elasticity is retained in the implanted segments, and there is no tendency to formation of a pseudointima, such as occurs with plastic cloth grafts. Furthermore, inasmuch as the material is impermeable, there is no chance for penetration of blood vessels from the adjacent tissues. The necessity for external vascularization of both homografts and plastic cloth grafts has been repeatedly emphasized.§

It is possible that the silicone rubber tubes used in these experiments were not completely free of decomposition products of the manufacturing process. However, this is thought unlikely by the manufacturer, whose tests reveal a quite pure silicone rubber product. The most probable cause of thrombosis is the presence of slight irregularities on the interior surface of the tubes. Work is under way toward the production of a smoother surface on silicone rubber.

SUMMARY

Silicone rubber was used as an aorta grafting material in 10 dogs, with only two

‡ Unpublished observations.

§ References 2 and 8.

Follow-Up of Silicone Rubber Grafts in Aorta

No. of Dogs	Course	Aortogram, 1 Wk.
1	Died first postoperative day; pneumonia; graft patent	.....
2	Hindquarter paralysis first postoperative day; dogs became weak and died on 3d and 4th postoperative days; grafts solidly thrombosed	.....
5	Dogs lived and had palpable femoral artery pulses; however, solidly thrombosed grafts at necropsy—1 wk. after insertion	Thrombosis of graft
1	Good femoral pulses, killed at 35 days; graft partially open; small thrombus at proximal suture line; no "endothelial" covering of graft material	Patent with good lumen
1	Killed at 46 days with good femoral pulses; graft patent except for small thrombus at proximal suture line; no attempt at "endothelization"	Patent with good lumen

grafts remaining patent longer than a few days. Despite the advantages of elasticity, high tensile strength, minimal tissue reactivity, and nonwettability, the silicone rubber preparation employed in this study had to be rejected for use in vascular grafting.

REFERENCES

1. Voorhees, A. B., Jr.; Jaretzki, A., III, and Blakemore, A. H.: Use of Tubes Constructed from Vinyon "N" Cloth in Bridging Arterial Defects, Ann. Surg. **135**:332-336, 1952.

2. Blakemore, A. H., and Voorhees, A. B., Jr.: Use of Tubes Constructed from Vinyon "N" Cloth in Bridging Arterial Defects: Experimental and Clinical, Ann. Surg. **140**:324-334, 1954.

3. Hufnagel, C. A., and Rabil, P.: Replacement of Arterial Segments, Utilizing Flexible Orlon Prostheses, A. M. A. Arch. Surg. **70**:105-110, 1955.

4. Hufnagel, C. A.: Permanent Intubation of the Thoracic Aorta, Arch. Surg. **54**:382-389, 1947.

5. Horsley, J. S.: Surgery of the Blood Vessels, St. Louis, C. V. Mosby Company, 1915.

6. MacGregor, R. R.: Silicones and Their Uses, New York, McGraw-Hill Book Company, Inc., 1954.

7. Brown, J. B.; Fryer, M. P., and Lu, M.: Polyvinyl and Silicone Compounds As Subcutaneous Prostheses: Laboratory and Clinical Investigation, A. M. A. Arch. Surg. **68**:744-751, 1954.

8. Egdahl, R. H.; Hume, D. M., and Schlang, H. A.: Plastic Venous Prostheses, S. Forum (1954) pp. 235-241, 1955.

Adrenal Cortical Steroids Following Elective Operations

Quantitative Studies in the Peripheral Plasma of 17-Hydroxy- and 17-Desoxycorticosteroids

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In the quest for a better evaluation of the indications for the therapeutic use of corticotropin (ACTH) and of adrenocortical steroids (cortisone, etc.) in surgical diseases, more about the nature and degree of the adrenocortical response to operation must be known. To this end, investigators have used a number of methods, including measurements of certain adrenocortical steroids and their metabolic products excreted in the urine, the eosinophile count of the peripheral blood, and the uric acid-creatinine ratio in the urine. The present report deals with a study of adrenocortical function based on quantitative determinations in the peripheral blood at intervals before and after operation of two groups of adrenocortical steroids. The two groups are (*a*) 17-hydroxycorticosteroids (17-OHCS), which have in common both an alpha ketol and a hydroxy group in the 17 position and include, among others, compound E (cortisone) and compound F, and (*b*) 17-desoxycorticosteroids (17-desoxy CS), which differ only in not having a hydroxy group in the 17 position and include, among others, compound B and compound Doc. A preliminary note of the present findings was reported at the Forum of the American College of Surgeons in 1952.

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PREVIOUS WORK

Although there is a large literature on the measurement of various adrenocortical steroids and their metabolic products in the urine, there have been very few observations made on the peripheral blood. Nelson and Sandberg [7] were probably the first to use a clinically feasible method in that they were able in relatively small samples of peripheral plasma to determine the concentration of the 17-OHCS. They and their associates have reported the following facts: Bliss and coworkers,[1] in 120 men and women, found concentrations of 17-OHCS in the peripheral venous plasma ranging from 1 to 34γ per 100 cc., with a mean for women of 15±6 and for men of 12±6. These values are somewhat higher and more variable than ours, as mentioned later and reported elsewhere.[14] Perkoff and others [8] found high values, of 28 to 65γ per 100 cc., in 91 patients, 12 just before death. A fall from 51γ to 3γ within one week was observed in a patient successfully treated for diabetic coma. Zero values were found in seven patients with Addison's disease and increased values, of 27γ to 103γ, in four patients with Cushing's disease before therapy. Sandberg and colleagues,[10] in 44 surgical cases studied for a maximum of six postoperative hours, found 17-OHCS levels which exceeded 30γ per 100 cc. in 29 and values above 100γ in 3. Tyler and others,[13] in 20 additional cases studied up to eight postoperative hours, found in nearly all operations of moderate to severe magnitude values higher than 30γ

per 100 cc., of which two reached 100γ, one a herniotomy done with use of spinal anesthesia.

Bondy and Altrock,[2] in single samples of blood obtained from the superior vena cava through the catheter technique in eight patients suffering various "stresses," none acute and only one of which was surgical (a patient with fracture of the femur), found only slight increases in 17-OHCS from an average normal of 16.3γ to a high of 26.7γ per 100 cc.

The 17-desoxy CS as a group, as far as we can determine, have not been measured. However, using a microchromatographic technique, Sweat and colleagues [11] found in peripheral blood 11γ and 4.9γ per 100 cc. of Compound F (a 17-OHCS) and Compound B (a 17-desoxy CS), respectively. Gornall and Macdonald [6] measured 17-OHCS and 17-desoxy CS together (total corticoids) and found in one patient on two occasions rather high values of 106γ and 104γ per 100 cc. (apparently all free unconjugated steroids), which rose to a maximum of only 200γ after infusion with corticotropin.

The conjugates of the 17-OHCS in the peripheral blood of human adults were found by Bongiovianni and others [3] to vary from 1.6γ to 9.7γ per 100 cc., rising after stress or corticotropin to a maximum of 30γ and after cortisone to a high of 97γ.

PROCEDURES USED

Selected for study were 24 adults undergoing elective surgical procedures, 19 of which were of moderate to extensive magnitude and 5 classed as "minimal," e. g., biopsy of a cervical node or abdominal exploration with biopsy. However, all operations were carried out with the use of general anesthesia, often with thiopental (Pentothal) sodium induction followed by nitrous oxide, oxygen, and ether. Samples of peripheral blood were obtained before the operation, and at 4 to 8, at 24, at 48, and at 72 hours thereafter. In six cases samples were obtained more frequently 2 to 17 hours after the incision was made. At about the same time, the eosinophiles in the peripheral blood were counted by the method of Randolph.[9]

Each blood sample, of 40 to 50 cc., was heparinized and centrifuged and the separated plasma stored in the deep freeze until ready for analysis. Two general analytical procedures were employed: the Porter-Silber reaction and a modified Mader-Buck (blue tetrazolium) reaction, by which Group I, or 17-OHCS, and Group 2, or 17-desoxy CS, were measured respectively. Detailed descriptions of these procedures and a discussion of their validity have been reported elsewhere,[14] including data on 42 "normal" adults. The values (in micrograms per 100 cc.) were as follows: for 17-OHCS, average 9.5, standard deviation 1.5, and for 17-desoxy CS, average 8.9, standard deviation 2.0. Glucuronic acid conjugates of the 17-OHCS group in 17 "normal" adults were (in micrograms per 100 cc.) as follows: average 16.8, standard deviation 1.5. Diurnal variations, also reported separately, showed a maximum rise at 8 a.m. to 18γ per 100 cc., a value which was well below the increase reported herein following severe operations.

FINDINGS

The findings are presented in two tables and two text figures and discussed under the following subheadings.

Day of Operation.—Since preliminary observations showed that the plasma steroids rose immediately after operation and tended to return to normal by 24 hours, frequent samples were taken in six cases at intervals during this period in order to determine, if possible, the time of maximum elevation. The findings are shown in Figure 1, in which it will be noted that the 17-OHCS rose in all cases, the highest being just under 80γ per 100 cc. The peak occurred at about 8 to 10 hours after the incision was made, which was about 4 to 7 hours after completion of the operation. By 24 hours, all values were back to the preoperative level. The 17-desoxy CS values behaved differently. Although they rose slightly within two hours after the beginning of the operation, the rise did not continue as was true of the 17-OHCS but fell and, indeed, in three cases completely disappeared from the blood at three to six

hours, only to reappear and show a secondary rise in two cases, apparently reaching a peak simultaneously with the 17-OHCS and then following with them a return to the preoperative level in 24 hours. This apparent dissociation in the pattern of change of these two groups of steroids was observed on other occasions as mentioned and discussed later.

The eosinophile count in Figure 1 dropped to zero by the sixth hour after the incision in 19 undergoing moderate to severe operative trauma (including the 6 shown in Figure 1) are shown in Table 1. The 17-OHCS, it will be noted, rose (at four to eight hours) in all but one case (No. 8) which will be discussed below. The range of increase was 30γ to 71γ per 100 cc., as compared with a normal preoperative range of 6γ to 20γ. This rise is to be compared with the absence of any rise in three out of five patients with "minimum" trauma as shown

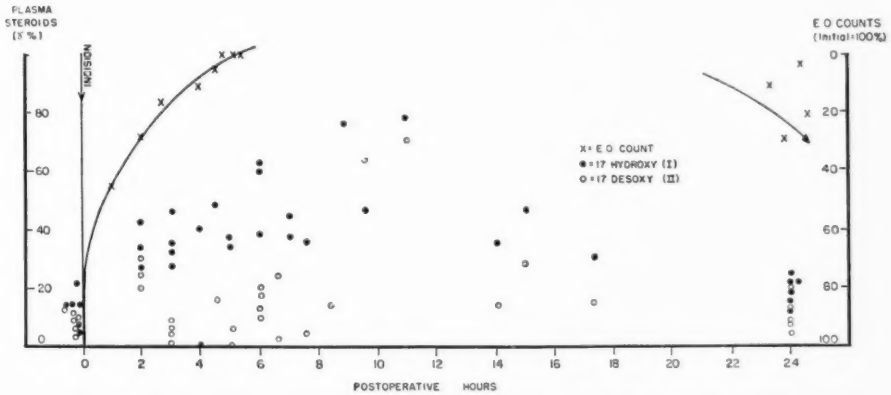

Fig. 1.—Eosinophile counts and plasma steroid levels during the day of operation. The findings above are from six patients ranging in age from 39 to 72 years. The operations were gastric resection, three; abdominoperineal resection, two; radical mastectomy, one. All had an uneventful recovery. Each round point represents one determination of plasma steroids. The solid points show 17-OHCS and open circles 17-desoxy CS, as described in the text. Each cross represents one eosinophile (E. O.) count arranged to show parallel changes with the plasma levels by reversing the scale as shown in the right ordinate.

Note that the fall in eosinophiles precedes the rise in 17-OHCS (I) and follows the return of the 17-OHCS(I) to normal. Note also the early and progressive rise in 17-OHCS(I) in contrast to the rise and fall in the 17-desoxy CS (II), a dissociation whose significance is discussed in the text.

was made, before the peak of 17-OHCS in the blood was reached. (A similar observation was made by Thorn, Jenkins and Laidlow,[12] who found that after a hysterectomy the maximum urinary output of 17-OHCS occurred several hours after the eosinophile counts had disappeared from the blood.) At 24 hours the eosinophile counts were still low but had begun to return to the preoperative level, in contrast to the corticosteroids, which had all returned to the preoperative level.

The First Three Postoperative Days.—In 24 patients, samples of blood were studied for three days after operation. The findings in Table 2. These findings, although different in many respects, are, in general, similar to those reported by Sandberg and others[10] and by Tyler and co-workers,[13] already mentioned.

Although the values for the 17-OHCS all fell at 24 hours, in 7 cases (Nos. 1, 5, 9, 11, 14, 15, and 16) they were still well above normal range (30γ per 100 cc. or higher). In three of the seven, even at 72 hours, they were slightly elevated (25γ per 100 cc. or more). All seven cases also showed the highest rise in the four-to-eight-hour sample after operation and thus presumably repre-

TABLE 1.—*Eosinophile Count (EO) and Peripheral Blood 17-Hydroxycorticosteroids (I) and 17-Desoxycorticosteroids (II) in Patients Undergoing Moderate to Severe Surgical Trauma*

	Preoperative			4 to 8 Hr. P. O.			24 Hr. P. O.			48 Hr. P. O.			72 Hr. P. O.		
Case No.*	Eo	I	II	Eo	I	II	Eo	I	II	Eo	I	II	Eo	I	II
1. C. S., 27, M D. U., G. R.	525	16	20	0	50	20	100	33	8	247	14	8	413	16	15
2. J. W., 26, M D. U., G. R.	247	6	25	81	38	30	16	22	20	92	19	7	160	14	11
3. W. Y., 35, M D. U., G. R.	69	17	13	1	41	14	22	24	10	72	17	9	94	19	3
4. N. R., 39, F Ca. S., G. R.	184	5	13	0	45	62	6	17	8	59	30	52	..	22	40
5. R. A., 56, F Gb., Ch.	88	10	9	0	50	7	13	44	8	15	21	3	25	23	6
6. D. B., 70, M Ca. R., AP. R.	475	8	8	3	34	7	125	10	2	238	19	0	300	17	6
7. J. W., 72, M Ca. R., AP. R.	303	9	12	0	63	15	41	24	12	175	55	11	269	24	12
8. H. M., 50, M Ca. R., AP. R.	77	16	12	..	20	6	128	28	1	178	28	3	..	..	..
9. B. R., 59, F Ca. R., AP. R.	81	21	12	6	57	6	17	38	4	61	24	0	53	21	10
10. G. B., 53, F Ca. R., AP. R.	537	16	24	19	70	60	250	17	5	326	25	9	619	26	21
11. H. H., 33, F U. C., R. R.	..	7	5	..	43	10	23	50	5	..	35	7	..	19	3
12. J. F., 47, M P. C., C. R.	44	16	4	0	36	26	3	18	9	100	19	2	241	18	8
13. A. B., 85, F Ca. C., C. R.	116	20	15	17	30	7	69	20	7	89	20	10	175	26	11
14. A. E., 72, F Ca. C., C. R.	..	17	3	19	50	4	9	42	9	59	36	1	88	25	12
15. W. W., 61, F Ca. C., C. R.	..	13	4	..	60	0	..	44	12	..	29	6	..	30	20
16. S. Z., 54, F Ca. C., C. R.	116	17	13	0	71	0	9	33	0	8	36	0	119	19	7
17. I. W., 68, F Ca. B., M.	166	15	9	0	45	32	63	25	9	..	35	2	131	20	12
18. M. R., 37, F A. T., T.	194	9	10	1	32	5	38	12	14	197	14	9	188	8	9
19. M. D., 35, F Th., T.	119	16	25	0	47	40	25	16	8	47	10	8	131	12	2

* The data after each case number refer to the patient's initials, age and sex. Key to the underlying abbreviations for diagnosis and operation is the following:

D. U.—duodenal ulcer
Ca. S., C., R., B.—carcinoma of stomach, colon, rectum, breast
P. C.—polyp of colon
U. C.—ulcerative colitis
Gb—gall-bladder disease
Th., A. T.—thyrotoxicosis, adenoma of thyroid
G. R., AP. R., C. R.—gastric, abdominoperineal, colon resection
R. R.—resection remaining rectum
T.—thyroidectomy
M.—radical mammectomy
Ch.—cholecystectomy

sented the most pronounced and persistent degree of adrenocortical stimulation, although other possible explanations are discussed later. In five of the seven, there was no clinical indication which could explain this more pronounced rise, but in two (Cases 9 and 14) the patients had severe postoperative complications and died. It is of interest to note that Sandberg and others [10] found the highest postoperative 17-OHCS value (148γ per 100 cc.) six hours after a cholecystojejunostomy in a patient with carcinoma of the pancreas, who died 36 hours later.

Postoperative complications occurred in only one other patient (Case 8), who showed moderate hypotension and persistent distention for several days, which gradually subsided with complete recovery. Curiously, this was the only patient of those undergoing significant operative trauma who failed to show a substantial rise in the 17-OHCS immediately or 24 and 48 hours after operation. The only unusual clinical feature discernible in this case was a rather pronounced apprehension and fear shown throughout the 10 preoperative days of diagnosis and preparation.

The 17-desoxy CS again showed quite a different postoperative response. In only five (Nos. 4, 10, 12, 17, and 19) out of the 19 cases listed in Table 1 was there a significant rise in the 4-to-8-hour postoperative sample, and in 4 of them the value then dropped below normal at 24, 48, or 72 hours. In all other cases, the 17-desoxy CS either did not rise at all or actually fell far below normal (in 12 cases to 5γ per 100 cc., or less, and in 4 cases to zero), unlike the 17-OHCS, case (No. 4) did the value for 17-desoxy CS rise at 24 and 48 hours (and then in a pronounced degree), in a patient who had the most extensive surgical procedure of all, a subtotal gastrectomy, splenectomy, and partial pancreatectomy. However, her postoperative course was uneventful.

Comparison of the relative steroid with the eosinophile values reveals substantial qualitative correlation similar to those shown in Figure 1. For example, the eosinophile

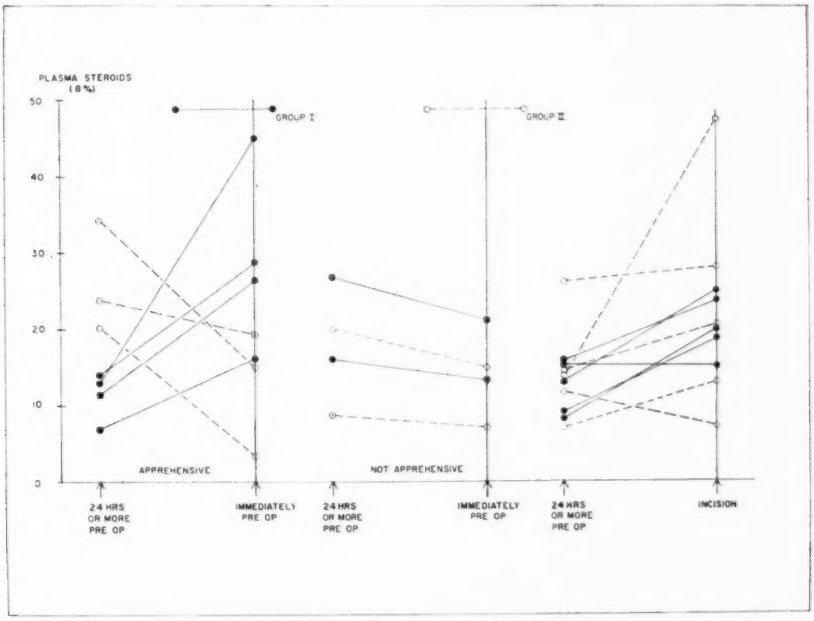

Fig. 2.—The effect of preoperative apprehension and induction of anesthesia on plasma steroids. Each point represents one plasma steroid determination (the solid circles Group I, or 17-OHCS, the open circles Group II, or 17-desoxy CS). Note on the left simultaneously a rise in the level of 17-OHCS, a fall in the 17-desoxy CS in three patients showing pronounced apprehension at the time the second sample was obtained. The controls are in the middle, two patients similarly studied except that they showed no apprehension. On the right note the slight changes (with one exception) in both groups as a result of the induction of general anesthesia.

which in no case fell below the preoperative value. Zero values for 17-desoxy CS were found at 4 to 8 hours in two cases, at 24 hours in one case, and at 48 hours in three cases. In one case (No. 16), no 17-desoxy CS were found in the 4-to-8-, 24- or 48-hour postoperative specimens, whereas the 17-OHCS rose to levels among the highest observed in the entire group. In only one counts (Table 1) were at zero or virtually zero in the 4-to-8-hour interval in all but four cases. However, these, too, might have revealed a complete eosinopenia had observations been made at later periods during the first 24 hours.

Of the five patients subjected to "minimal" trauma (Table 2), three showed practically no increase in the 17-OHCS; of the two who

did, one (No. 24) suffered persistent fever of unexplained origin due presumably to Hodgkin's disease and the other (No. 23) had extensive carcinoma but may have had more tissue trauma in terms of more vigorous abdominal palpation by several members of the operative team than was true in the other two cases (Nos. 20 and 21) with similar lesions but in whom there was no postoperative increase in the 17-OHCS. The 17-desoxy CS in these cases were in general fairly high but showed no increase after operation. In those that fell the level was never far below normal (lowest, 7γ per 100 cc.) and there were no zero values as was true of the cases listed in Table 1.

The Effects of Apprehension.—In five patients, plasma levels 24 or more hours before were compared with those immediately before operation. The findings are shown in Figure 2. Of special interest is not the rise in the 17-OHCS in the three apprehensive patients, which is probably to be expected in view of the psychic stimulation of the pituitary, but the simultaneous fall in the 17-desoxy CS. This is another example of a pattern of dissociation in the behavior of these two groups of hormones, a phenomenon which has already been noted in previous observations already mentioned.

COMMENT

The present communication records observations made on the peripheral plasma levels of two groups of adrenocortical steroids before and after operation. The significance of these findings as a measure of postoperative adrenocortical stimulation depends upon a number of considerations. One of these is the pertinent question as to the true nature of the substances measured. While the methods used, as discussed in a previous paper,[14] are accurate and reproducible, do the values really represent biologically active steroids? This query applies, of course, to all steroid determinations by chemical methods and to most of the studies by others in this field. It cannot be answered until each of the specific steroids measured by the group reactions used can be chemically identified and their biological activity determined.

While not entirely proved, we believe that the methods used in this work do measure the concentration in the peripheral blood of the 17-OHCS as well as of the 17-desoxy CS, without reference to biological activity. Of the two, there is probably greater specificity in the former values, largely because of the specificity of the Porter-Silber reaction which is used in its determination. This reaction measures all adrenocortical steroids containing both an alpha ketol and a 17-hydroxy group (dihydroxyacetone), thus including compounds of the types E, F, S, dihydro E and F, and tetrahydro E and F. Though not as specific, we believe that the reactions used for the 17-desoxy CS measure all steroids having an alpha ketol but no 17-hydroxy group, thus including compounds of the type A, B, Doc, aldosterone, and certain of the pregnane series. If the steroids measured are largely compound F and compound B respectively, the interest of the present observations would be considerably enhanced.

Do the prompt increases in the blood levels of the 17-OHCS after operation as herein reported indicate true adrenocortical stimulation? While this would appear to be true, other possible factors may be mentioned and discussed. These deal with the possibility that the rise in the blood level may be due to (1) a diminution in the rate of peripheral tissue utilization and/or hepatic conjugation and metabolic conversion of normally secreted steroids, thus permitting their accumulation in the blood, and (2) retention of normally secreted steroids resulting from a diminution in the rate of renal clearance.

That a diminution in the rate of peripheral tissue utilization and hepatic conjugation and metabolic conversion is not responsible is suggested by the following observations which we hope to describe in detail in a later report. In three patients, compound F was infused before and 24 hours after either unilateral adrenalectomy for advanced carcinoma of the breast. No difference was observed in the rise and fall of the 17-

OHCS or in the curve of the 17-desoxy CS. The same observations before and four days after an abdominoperineal resection for carcinoma of the rectum also showed no difference. Moreover, no difference was observed in the rate of appearance and disappearance of glucuronic conjugates following these compound-F infusions. In five somewhat similar experiments recently described by Sandberg and others,[10] no difference in the rate of removal of 17-OHCS was observed in two and a diminished rate in three. Much more significant is the observation we made in one patient who after cholecystectomy showed a 17-fold increase in total 17-OHCS (free plus glucuronic acid conjugates) as compared with a usual fivefold increase in the free steroids. In this instance the increase in the free steroids obviously could not be due to diminished conjugation. Indeed, these findings, which we hope to report in detail later, suggest that the rise of the free steroids in the blood after operation gives an incomplete picture of the degree of adrenocortical stimulation. However, many more observations are obviously needed, particularly in view of the recent studies by Brown and colleagues,[1] showing that hepatic impairment definitely slows the disappearance rate of injected compound F, and by Tyler and others,[13] showing a correlation between postoperative blood levels and hepatic impairment.

That a diminution in renal clearance is responsible for the postoperative increases in plasma levels of 17-OHCS found herein cannot be stated on the basis of present knowledge. While it is true that postoperative increases in the urinary excretion of various corticoids have been observed by most workers and even with specifically measured "total" 17-OHCS as recently reported by Thorn, Jenkins, and Laidlow,[12] the influence of a diminished renal clearance on blood levels remains unsolved. We are now engaged in studying this factor with special reference to its quantitative significance in relation to the changes observed herein.

TABLE 2.—*Eosinophile Count (EO) and Peripheral Blood 17-Hydroxycorticosteroids (I) and 17-Desoxycorticosteroids (II) in Patients Undergoing Slight Surgical Trauma*

	Preoperative			4 to 8 Hr. P. O.			24 Hr. P. O.			48 Hr. P. O.			72 Hr. P. O.		
Case No.*	Eo	I	II	Eo	I	II	Eo	I	II	Eo	I	II	Eo	I	II
20. M. M., 82, F Ca. Gb., B.	156	34	41	69	29	46	91	26	20	85	34	12	104	33	9
21. E. S., 42, F Ca. S., B.	92	30	12	10	19	12	112	15	9	..	21	9	..	..	..
22. M. D., 28, F H. D., L. N.	..	14	..	..	8	..	86	16	..	..	..	..	..	..	..
23. C. S., 42, M Ca. S., B.	41	23	15	0	58	20	0	21	7	9	30	11	28	14	7
24. G. Y., 52, F H. D., B.	11	28	18	1	57	30	26	80	21	58	26	21	24	21	20

* The data after each case number refer to the patient's initials, age and sex. Key to the underlying abbreviations for diagnosis and operation is as follows:
Ca. Gb., S.—carcinoma of gall-bladder and/or stomach with widespread metastases
H. D.—Hodgkins' disease
B.—biopsy during abdominal exploration
L. N.—removal of cervical lymph node

As to the relative influence of tissue damage and of anesthesia on the postoperative rise in 17-OHCS, the present findings (compare Tables 1 and 2) would seem to attribute more to the former than to the latter. That the type of anesthesia is not important is indicated in the data by Sandberg and others,[10] who found that spinal anesthesia was followed by just as great a rise as general anesthesia. Induction of general anesthesia itself apparently has little influence, as shown by our findings in five patients (Fig. 2) in whom only a slight increase (8γ to 18γ, 9γ to 16γ, 12γ to 22γ, 15γ to 15γ, 18γ to 24γ per 100 cc.) was observed in the 17-OHCS level before and immediately after the patient was completely anesthetized. As to tissue trauma itself,

Sandberg and co-workers [10] felt, on the basis of their findings, that the degree of increase in 17-OHCS after operation was "roughly proportional to the duration and severity of the operative procedure." Although we found no increase in those subjected to minimum trauma (Table 2), we could draw no correlation between the blood levels and the degree of tissue damage among those subjected to moderate to severe operation (Table 1). Further study is obviously needed, with more data on the influence of both hepatic and renal function.

The unusual findings in regard to 17-desoxy CS are of considerable interest and possible importance. Unlike the uniform rise in 17-OHCS after operations of moderate to severe magnitude (Table 1), in only five cases was there any increase in the level of 17-desoxy CS, and then all but one at four to eight hours only. More striking was the frequency of low and several zero values after operation. A similar difference in the plasma level of the two groups of steroids was also noted as a result of preoperative apprehension. These findings seem significant, since in "normal" peripheral blood, as already mentioned we found equal levels for 17-OHCS and 17-desoxy CS, i. e., 9.5γ and 8.9γ per 100 cc. respectively.

Although the present observations certainly show a similar pattern of dissociation in the behavior of the two groups of steroids measured under conditions of stress, they do not answer the question as to the cause. Is the tendency for 17-desoxy CS to fall and to disappear after stress due to an increase in its conjugation by the liver and other metabolic conversions by peripheral tissues or to a decrease in its actual secretion by the adrenal gland? As to the former possibility, methods are not at present available for the quantitative estimation of the conjugated 17-desoxy CS as they are for the conjugated 17-OHCS. Infusions of compound B similar to those already mentioned with compound F before and after operation might be informative

The second possibility, i. e., that the lower values for the 17-desoxy CS in the peripheral blood after stress were due to a decrease in the secretion of these steroids, seems likely in view of measurements we made on human adrenal vein blood obtained during operation. Extremely high values were, of course, found for both the 17-OHCS and 17-desoxy CS (944γ and 390γ per 100 cc. respectively). However, the proportionately lower level of the 17-desoxy CS as compared with the peripheral blood certainly suggests that they are secreted at a lower rate than the 17-OHCS. This inference is also supported by the data of Sweat and others,[11] who found a similar difference between peripheral and adrenal vein blood, i. e., the proportions between compound F, a 17-OHCS, and compound B, a 17-desoxy CS, were two to one and five to one respectively. Somewhat similar inferences emerge from the recent findings of Farrell and others,[5] which suggest that the secretion of one of the 17-desoxy CS (aldosterone) is probably not under anterior pituitary control, inasmuch as the concentration of this steroid in the adrenal vein blood of dogs was not influenced by either corticotropin infusion or hypophysectomy, procedures which led to an increase and decrease respectively in the concentration of 17-OHCS. In corticotropin infusions in the human we have always observed, as have others, an increase in 17-OHCS but frequently no change in 17-desoxy CS. Thus it would appear that, while the 17-OHCS are undoubtedly secreted at an increased rate as a result of pituitary stimulation following operation, it is probably that the 17-desoxy CS are not similarly under pituitary control.

Therapeutic implications from the present data must necessarily be purely speculative. It would seem, however, that the use of cortisone or compound F, which are 17-OHCS, might depend not only on their own action but on the effect they have on the metabolism and/or secretion of compound B, Doc, and others of the 17-desoxy CS. Inasmuch as several steroids are secreted by the adrenal

cortex, each with presumably different physiologic influence, more information about more of them is needed. The present study adds such information regarding the group of 17-desoxy CS, many of which are certainly as active as, or even more active than, many of the 17-OHCS and perhaps just as important from the therapeutic point of view.

SUMMARY

Concentrations of two groups of adrenocortical steroids, i. e., 17-hydroxycorticosteroids and 17-desoxycorticosteroids have been measured at frequent intervals in the peripheral plasma of 24 patients before and after surgical procedures, with techniques which require only 20 ml. of plasma for both determinations.

A rising concentration of the 17-hydroxycorticosteroids was observed in the plasma of all but one patient after operations of moderate or severe magnitude, reaching a peak in most cases in about 8 to 12 hours and falling to the preoperative levels, usually at 24 or by 72 hours.

The eosinophiles in the peripheral blood fell to zero before the maximum rise in 17-hydroxycorticosteroids was reached and returned subsequent to the fall in the latter to the preoperative level.

The degree of the rise in 17-hydroxycorticosteroids varied but could not be correlated with the preoperative state or with the magnitude of the operation, except that in three of five patients subjected to the same general anesthesia but to a "minimum" operation there was no rise in this group of steroids.

The 17-desoxycorticosteroids behaved quite differently in that a postoperative rise was found in only a few cases. In the others there was either no change or a fall, sometimes to zero. In a few observations, preoperative apprehension was accompanied by an increase in the 17-hydroxycorticosteroids and a simultaneous decrease in the 17-desoxycorticosteroids. These findings suggest a dissociation in the pattern of behavior of the two groups of adrenocortical steroids to stress, since each is present in similar concentrations in the peripheral blood under normal conditions.

The significance of the present findings in terms of the adrenocortical stimulation after operation is discussed. The suggestion is made, based on peripheral plasma levels of the adrenocortical steroids as measured herein, that the adrenotropic effect of the anterior pituitary after operation leads to an increase in the secretion of 17-hydroxycorticosteroids but is with much less or no influence on the secretion of 17-desoxycorticosteroids. The importance of information in regard to the latter group of steroids in the therapeutic use of both groups is emphasized.

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REFERENCES

1. Bliss, E. L.; Sandberg, A. A.; Nelson, D. H., and Eik-Nes, K.: J. Clin. Invest. **32**:818, 1953.
2. Bondy, P. K., and Altrock, J. R.: J. Clin. Invest. **32**:703, 1953.
3. Bongiovanni, A. M.; Eberlein, W. R.; Grumbach, M. M.; VanWyk, J. J., and Clayton, G.: Proc. Soc. Exper. Biol. & Med. **87**:282, 1954.
4. Brown, H.; Willardson, D. G.; Samuels, L. T., and Tyler, F. H.: J. Clin. Invest. **33**:1524, 1954.
5. Farrell, G. L.; Royce, P. C.; Rauschkolb, E. W., and Hirschmann, H.: Proc. Soc. Exper. Biol. & Med. **87**:141, 1954.
6. Gornall, A. G., and MacDonald, M. P.: J. Biol. Chem. **201**:279, 1953.
7. Nelson, D. H.; Sandberg, A. A.; Palmer, J. G., and Tyler, F. H.: J. Clin. Invest. **31**:843, 1952.
8. Perkoff, G. T.; Sandberg, A. A.; Nelson, D. H., and Tyler, F. H.: A. M. A. Arch. Int. Med. **93**:1, 1954.
9. Randolph, T. G.: J. Lab. & Clin. Med. **34**: 1696, 1949.
10. Sandberg, A. A.; Eik-Nes, K.; Samuels, L. T., and Tyler, F. H.: J. Clin. Invest. **33**:1509, 1954.
11. Sweat, M. L.; Abbott, W. E.; Jeffries, W. McK., and Bliss, E. L.: Fed. Proc. **12**:141, 1953.
12. Thorn, G. W.; Jenkins, D., and Laidlow, J. C.: Recent Progress in Hormone Research: The Laurentian Conference, New York, 1953, Academic Press, Vol. 8, p. 210.
13. Tyler, F. H.; Schmidt, C. D.; Eik-Nes, K.; Brown, H., and Samuels, L. T.: J. Clin. Invest. **33**:1517, 1954.
14. Weichselbaum, T. E., and Margraf, H. W.: J. Clin. Endocrinol. **15**:970, 1955.

A Radical Combined Operation for Cancer of the Head and Neck

A Study of the Operative Mortality and Morbidity

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and
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The purpose of this report is to record the operative mortality and morbidity associated with a specific major operation of the head and neck, consisting of a radical neck dissection, resection of a portion of the mandible, and excision of the intraoral primary lesion, all performed in continuity ("commando" *).

The study underscores the fact that the prohibitive mortality and morbidity formerly associated with such procedures (during the 1920's and 1930's) no longer exist. Advances in medicine during the last two decades, particularly chemotherapy, antibiotics, blood banks, and newer techniques of anesthesia and surgery have made a low mortality and morbidity possible.

CLINICAL MATERIAL

The cases in this study represent all the "commandos" performed at Memorial Center, New York, during the one-year period from Jan. 1, 1950, through Dec. 31, 1950. There were 114 patients so treated during this period.

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* For want of a better term, these operations were given the name "commando" by the house staff at The Memorial Center, New York, in 1942, at the time of the combined Commando operations against Dieppe.

No cases were excluded, and there was no attempt at selection. The Table shows the sites of origin of the primary tumor in the series.

Of the 114, the youngest patient was 28 and the oldest 87. More than 50% were in the 60 to 70 age group (Fig. 1).

Almost half of the patients had preoperative evidence of cardiovascular dysfunction, many with signs of myocardial damage. Despite these findings and associated operative risk, no patient was denied surgery—their other alternative being death from untreated cancer. The poor-risk patients were brought into the best possible condition prior to surgery.

Only 75 of the 114 had received no previous therapy. Of those previously treated, 9 had surgery, 24 radiation, and 4 both surgery and radiation. (In two cases, the type of previous treatment was unknown.) All those previously treated had recurrent disease. This history of the previous treatment is important in evaluating the results of this study, since it is generally accepted that unsuccessful treatment by surgery or radiation makes subsequent surgery not only more difficult but

Site of Primary Lesion

Anatomic Site of Primary Lesion	Cases, No.
Lip	2
Mucosa of cheek	9
Gingiva	20
Palate	2
Floor of mouth	26
Tongue	33
Tonsil	16
Salivary gland	3
Pharyngeal wall	1
Nasopharynx	1
Mixed tumor of soft palate	1
Total number of cases	114

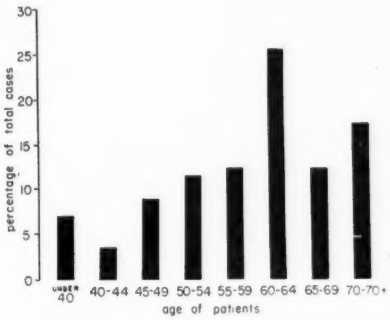

Fig. 1 - DISTRIBUTION OF PATIENTS BY AGE GROUPS

also more extensive, therefore followed by a greater postoperative morbidity.

EXTENT OF SURGICAL PROCEDURE

The "commando" is a lengthy procedure. Operating time in this series ranged from slightly less than three hours (three cases) to over six hours (six cases). The median was 4 + hours in 92% of the cases. Patients were given from 500 to 3500 cc. of blood, the average transfusion being about 1500 cc.

Postoperative hazards include temporary interference with breathing, which can lead to respiratory complications, as well as temporary interference with speech and swallowing. There is also the possibility of uncertain wound healing.

OPERATIVE MORTALITY

Despite the advanced age of the majority of the patients, the poor preoperative condition, and the extent and duration of the procedures, the operative mortality rate was extremely low.

By "operative mortality" we refer to those deaths occurring in the hospital within 30 days after operation. In this series, there was one death due to ventricular fibrillation on the sixth postoperative day. This gives an "operative mortality" of 0.88%.

There were, however, three other hospital deaths. One occurred on the 62nd postoperative day following surgery for perforated ulcer and gastrointestinal hemorrhage. Another occurred on the 73d postoperative day and the third on the 88th postoperative day. (The causes of death in the latter two cases were not clearly defined.) If one included these three hospital deaths in an even broader definition of "operative mortality," the rate would still be low, specifically 3.5%.

MORBIDITY

The low morbidity following the radical combined operation for cancer of the head and neck is also impressive, as the following data will bear out.

Postoperative Pain.—Despite the magnitude of the surgery, postoperative pain is not a problem. Only five patients reported moderate discomfort, and none complained of severe pain. Acetylsalicylic acid or acetylsalicylic acid-acetophenetidin-caffeine was adequate for postoperative analgesia in 94.7% of the cases. This notable absence of pain is attributable in part to the cutting of the sensory branches of the cervical plexus during the operation.

Ambulation.—Of the 114 patients, 110 were ambulated on the first postoperative day. No patient was bedridden.

Temperature Elevation.—The oral cavity, a highly contaminated area, is impossible to sterilize. Since it is part of the operative field in the "commando," one would normally anticipate infection and rise in temperature. Our study disavows this. The median temperature rise was to 102.2 F, occurring on the first postoperative day, followed by a steady drop, and ultimately a return to normal on

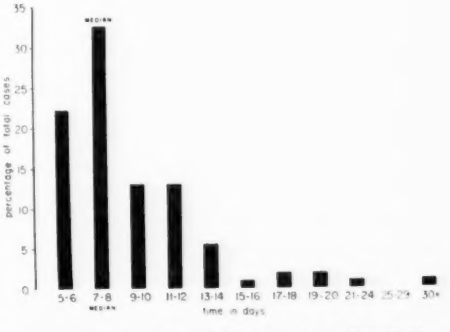

Fig. 2 - TIME TAKEN FOR RETURN TO NORMAL TEMPERATURE

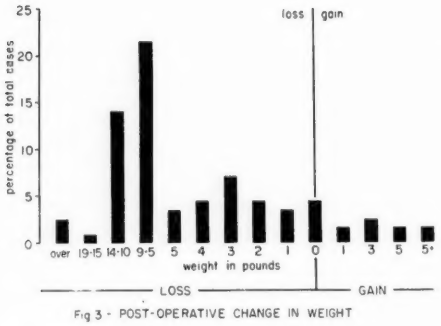

Fig 3 - POST-OPERATIVE CHANGE IN WEIGHT

the seventh or eighth day (Fig. 2). The routine systemic use of antibiotics in high dosage is responsible for this benign febrile pattern.

Removal of Tracheostomy Tube.—The restriction of tongue movement which follows removal of the mandible and the almost invariable intraoral and pharyngeal edema often seriously obstruct the airway. Tracheostomy is therefore routinely performed. The tracheostomy also permits ready aspiration of tracheal secretions and thus avoids respiratory infection secondary to obstruction. The tracheostomy is temporary, and the tube is removed when there is no longer any obstruction to normal respiration. In 80% of the patients the tube was removed by the 10th day. The sixth postoperative day was the median for tube removal.

Feeding.—Because this extensive intraoral surgery involves the removal of a portion of the mandible and, very often, removal of a large portion of tongue and pharyngeal wall, patients are unable to swallow an adequate daily intake of fluids and solids for a short time after the operation. Dietary deficiency can be prevented by feedings through a 16 F. urethral catheter threaded through the nose into the esophagus. Patients are fed a liquid mixture of high caloric value and rich in proteins and vitamins until they are capable of taking sufficient nourishment by themselves. Although some patients were able to swallow after four days, the median duration for tube feeding was nine days.

Despite reliance on tube feeding alone, inanition was not shown to be a problem. Twelve per cent of the cases either gained or maintained their weight. Of those losing weight, the usual loss was only 5 to 9 lb. (This is no greater than the loss any patient may incur during an average hospital stay, regrdless of the nature of the surgery performed) (Fig. 3).

Local Complications.—Even though the oral cavity cannot be rendered sterile, there were surprisingly few wound complications: 19 patients had slight necrosis of the suture line; 18 patients had disruption of the suture line; 9 developed wound infections; 5 developed wound collections, and 6 developed fistulas.

Local complications alone were responsible for delay in discharge from the hospital in only 13 patients.

Systemic Complications.—The most frequent systemic complication were those associated with the respiratory tract, specifically pneumonitis and atelectasis. These occurred in 23 cases but only in 12 cases were responsible for delay in discharge from the hospital.

The fear of cardiovascular complications frequently makes patients reluctant to submit to major surgical procedures. In this series, excluding the patient who died on the sixth postoperative day from ventricular fibrillation, there were only two postoperative cardiovascular complications despite the fact that 52 had reported preoperative cardiovascular disease. These two complications.

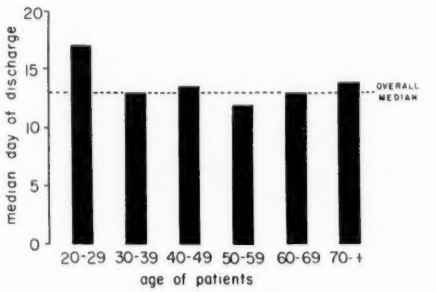

Fig. 4 - MEDIAN DAY OF DISCHARGE FOR DIFFERENT AGE GROUPS

furthermore, were of a minor nature and did not postpone the patient's discharge date.

Length of Hospital Stay.—Prior to the last two decades, failure of primary wound healing, infection, fistula, or respiratory complications were common. Today, these complications are infrequent, and as a result hospitalization is not unduly long. While some patients were discharged as early as the 7th or 8th day, the median day of discharge was the 13th. This was true even in the older age groups (Fig. 4). Reasons for the increase in hospital stay were as follows: delayed wound healing, in 13 patients; delay in removal of tracheostomy tube, in 8 patients, and of feeding tube, in 13; systemic complications, in 10.

At discharge, 73% of the patients were in good general condition and 17% in fair condition. The wounds were completely healed in 56% and almost fully healed in 20%. After discharge, all returned either to the clinic or to private offices for further care, where no subsequent difficulties were encountered.

SUMMARY AND CONCLUSIONS

This study of the 114 radical combined operations for cancer of the head and neck performed at the Memorial Hospital, New York, in 1950, underscores the compelling fact that this extensive radical surgery can be performed with a remarkably low mortality and morbidity, even in elderly and debilitated patients.

The operaitve mortality rate was only 0.88%. Postoperative morbidity was also extremely low, viewed both from the subjective attitude of the patients and from the incidence of postoperative local and systemic complications, the length of hospital stay, feeding problems, and ambulation.

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REFERENCES

1. Crile, G. W.: Excision of Cancer of the Head and Neck, with Special Reference to the Plan of Dissection Based on 132 Operations, J. A. M. A. **47**:1780-1786, 1906.

2. Crile, G. W.: Carcinoma of the Jaws, Tongue, Cheek, and Lips: General Principles Involved in Operations and Results Obtained at Cleveland Clinic, Surg., Gynec. & Obst. **36**:159-162, 1923.

3. Martin, H.; Del Valle, B.; Ehrlich, H., and Cahan, W. G.: Neck Dissection; Cancer **4**:441-499, 1951.

4. Martin, H.: Radical Surgery in Cancer of the Head and Neck, S. Clin. North America **33**: 329-350, 1953.

Pancreatic Ductal Decompression in Chronic Pancreatitis with Fistula

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Somogyi's contribution of the test for serum amylase [1] has made possible the more frequent diagnosis of pancreatitis, with the result that nonsurgical treatment for the disease can be used oftener. The edematous type of pancreatitis, which is found more commonly and which may manifest itself in repeated attacks, usually responds well to conservative treatment. The more fulminating hemorrhagic type in which there is free fluid in the peritoneal cavity still carries a high mortality.

The recognition of pancreatic duct obstruction, whether it be secondary to obstruction at the ampulla of Vater, due to extrinsic compression of the ampulla or pancreatic duct, or within the pancreatic duct itself, as a factor in the cause of pancreatitis has gradually led to measures directed toward decompression of the pancreatic ductal system or removal of the element of obstruction. Removal of a calculus from the common bile duct and Doubilet's operation of sphincterotomy [2] are two measures for relief of obstruction in the ampullary region. The internal drainage of a pseudocyst by cystoenterostomy [3] is a means of decompression of obstructed pancreatic secretion. Shanahan recently described the cure of a chronic external pancreatic fistula by implantation of the fistula into the jejunum.[4] Berens, Baggenstoss, and Gray reported ductal dilatation in a number of cases of chronic pancreatitis [5] and suggested surgical retrograde decompression as a method of treatment. DuVal described caudal pancreaticojejunostomy in two cases of chronic pancreatitis.[6] His procedure consists of transection of the pancreas at the junction of body and tail and end-to-end anastomosis between the cut end of the body of the pancreas and a defunctionalized limb of upper jejunum.

There follows a case report in which a somewhat similar technique was used in treatment of a chronic pancreatic fistula.

REPORT OF A CASE

A 39-year-old white man was admitted to the Queen's Hospital, Honolulu, on Feb. 14, 1952, with the complaints of severe epigastric pain and vomiting of eight hours' duration. He had been drinking whisky heavily for several days and gave a history of chronic alcoholism. His vital signs were normal, but there were moderate generalized tenderness and rigidity of the abdomen. Serum amylase and urine amylase determinations both revealed more than 1600 Somogyi units. A diagnosis of acute pancreatitis was made, and conservative treatment was instituted. On the day after admission, delirium tremens developed and the patient was transferred to a psychiatric ward. After several days he became asymptomatic, and he was discharged from the hospital on Feb. 22.

Nine days later, on March 3, he was readmitted with recurrent epigastric pain and tenderness. An ill-defined tender mass, 8 cm. in diameter, was palpable in the right side of the epigastrium. A serum amylase study revealed 450 Somogyi units. The possibility of the development of a pseudocyst was considered. Treatment was conservative, and the patient was discharged much improved after four days.

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A third admission occurred on April 10, when he again had severe epigastric pain, nausea, and abdominal distention. A serum amylase determination revealed 540 units. Over a period of nine days, the patient developed increased abdominal distention, with a palpable epigastric mass. Laparotomy, through an upper abdominal transverse incision, revealed subhepatic and subdiaphragmatic collections of cloudy grayish-yellow fluid, about 300 cc. in volume, enclosed by a friable, fibrinous capsule. One cubic centimeter of this fluid digested 1000 cc. of starch solution. Rubber tissue drains were placed into the areas of fluid collection and brought out through the wound on the anterior abdominal wall. A pancreatic fistula developed; the flow of secretion gradually slowed and finally ceased. The patient was discharged to a convalescent hospital on May 12.

He was readmitted to the Queen's Hospital three days later because of recurrent epigastric pain and generalized abdominal distention. On May 19, a recurrent subhepatic pseudocyst, which was poorly encapsulated, was marsupialized to the exterior at the site of the old incision. A jejunostomy was performed for purposes of feeding. Afterward, severe excoriation of the skin occurred about the site of drainage from the pseudocyst, and a fecal fistula from the transverse colon developed. The patient was uncooperative in regard to treatment, and he became markedly malnourished. Because of a progressively downhill course, laparotomy through the left flank to avoid the site of the combined pancreatic and fecal fistulas was finally resorted to on June 27, 1952. The tail of the pancreas was freed and the distal 5 cm. of it excised. The main pancreatic duct in the cut end of the remaining portion of the gland was catheterized with a No. 20 polyethylene tube for a distance of 10 cm. toward the head of the pancreas. The cut end of the gland, with tube in place, was anastomosed to a loop of jejunum 20 cm. from the ligament of Treitz with two rows of interrupted 0000 nonabsorbable surgical (silk) sutures. An additional jejunojejunostomy was performed between the afferent and efferent segments of the jejunum. The clear colorless drainage of the pancreatic fistula ceased immediately, and the skin excortiation soon disappeared. The patient improved markedly, and, after closure of the fecal fistula, he was discharged from the hospital on Aug. 13, 1952. The segment of pancreas that was excised was firm in consistency. Microscopic examination revealed marked fibrosis, especially in the interlobar and interacinar areas, consistent with a diagnosis of chronic pancreatitis.

Since his discharge, the patient has been able to work and has been almost symptom-free. A ventral hernia at the site of the previous pancreatic fistula was repaired in April, 1953, and in August, 1954, he was readmitted to the hospital because of epigastric pain following the ingestion of about 1 pt. of whisky. The examination was essentially negative, and he was asymptomatic after 24 hours. His nutritional status has remained excellent.

In the above case, the initial treatment of marsupialization for what was thought to be a pseudocyst that was amenable to surgical therapy resulted in the development of an intractable pancreatic fistula which was complicated later by a fecal fistula and progressive debility. As a last therapeutic resort, transection of the tail of the pancreas was performed and pancreaticojejunostomy executed as a means of sidetracking the flow of pancreatic secretion away from the fistula.

SUMMARY

The concept of pancreatic duct obstruction as the cause of pancreatitis is presented. Various methods of decompression of the pancreatic ductal system are mentioned. A case report describing the use of ductal decompression by pancreaticojejunostomy for a chronic pancreatic fistula is presented.

REFERENCES

1. Somogyi, M.: Micromethods for Estimation of Diastase, J. Biol. Chem. **125**:399, 1938.

2. Doubilet, H., and Mulholland, J. H.: Recurrent Acute Pancreatitis: Observations on Etiology and Surgical Treatment, Ann. Surg. **128**:609, 1948.

3. Van Meter, J. F., and Floyd, J. B., Jr.: Cyst of the Pancreas: Further Observations on Treatment by Internal Drainage, Am. Surgeon **18**:1005, 1952.

4. Shanahan, T. H.: Cure of Pancreatic Fistula by Pancreaticojejunostomy, Am. J. Surg. **88**:516, 1954.

5. Berens, J. J.; Baggenstoss, A. H., and Gray, H. K.: Ductal Changes in Chronic Pancreatitis, A. M. A. Arch. Surg. **68**:723, 1954.

6. DuVal, M. K., Jr.: Caudal Pancreatico-Jejunostomy for Chronic Relapsing Pancreatitis, Ann. Surg. **140**:775, 1954.

Glomus Tumors

An Analysis of Twenty-Five Cases

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Glomus tumors were first described in 1812 by Wood,[1] who observed them clinically to be small, bluish, benign subcutaneous nodules of slow growth associated with acute intermittent, spasmodic pain and tenderness. One hundred twelve years later, Masson [2] reported a microscopic description of this tumor, which was then first recognized as originating from a glomus.

The first glomus tumor case reported in the United States was described by Mason and Weil [3] in 1934. Immediately afterward case reports appeared rapidly, until at present well over 300 cases have been reported.

While case reports are now by no means rare, this tumor is still regarded as an uncommon lesion by most clinicians. We feel that this condition is not so rare as is commonly supposed, but rather that many cases are misdiagnosed or overlooked because of lack of familiarity with the lesion.

NORMAL GLOMUS

The normal glomus is an end-organ apparatus which consists of a remarkable type of arteriovenous anastomosis functioning without an intermediary capillary bed. The histology of this structure has been accurately recorded by Popoff [4] and Masson,[2] who described the glomus as consisting of an afferent artery which is connected directly to a primary collecting vein by a tortuous anastomotic vessel termed the Sucquet-Hoyer canal. This canal is endothelial-lined and surrounded by smooth muscle fibers and glomal cells that are covered by a delicate collagenous material through which run numerous nonmyelinated nerve fibers. This glomic system is always found in the stratum reticulare of the skin. Rarely does it exceed 1 mm.

In order to arrive at a rough estimate of the number of glomic structures in normal skin, serial sections of the great toe were obtained by Popoff,[4] who found 18 glomic structures on the ventral surface, 10 on the lateral surface, 24 in the nail bed, and 12 in the nail matrix. Normally, glomic structures are distributed widely over the body but are somewhat more numerous on the extremities, particularly on the fingers and toes. They are absent or rare in the newborn infant.

The function of the glomus is thought to be related to the control of the arteriovenous circulation of the skin. Through this direct shunt, without the intervention of capillaries, the body can apparently regulate the local and general body temperature by the dissipation or conservation of heat. The control of the glomus is by the autonomic nervous system, which may explain the pain, temperature changes, and sweating often associated with this tumor.

TUMORS OF THE GLOMUS

Various names have been given in the past to the glomus tumor. Before there was an accurate pathological description practitioners knew them as "painful cutaneous tubercles." [1] The name "glomangioma" has been suggested by Bailey, and the *Quarterly Cumulative Index* originally classified these tumors as angioneuromyomas.

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The typical glomus tumor is generally a single tumor.[5] In none of our cases did we note the existence of multiple nodules. However, the incidence of multiple individual tumors in the same patient has been recorded in as high as 5% of cases, and the occurrence of as many as 48 discrete lesions on one patient has been described.*

The color of the tumor is most frequently a deep red to purple or blue, depending on changes in skin temperature. The tumor is usually small, rarely more than 2 to 5 mm. in size, and consists of a slightly raised, bluish, tender subcutaneous nodule.[8] The subungual area is a favorite site of occurrence; however, this tumor occasionally may be so small as to be missed by inspection or palpation, and only the symptom of severe persistent pain in a minute area may lead to the diagnosis by excision and microscopic examination of the involved site.[9]

Clinically, glomus tumor pain is pathognomonic and present in a high percentage of all cases.[10] There is exquisite tenderness to touch. Even slight pressure may cause lancinating or radiating pain. The pain may recur with temperature changes or changes in position of the lesion. When the lesion is subungual, the nail is frequently thickened and ridged. Increased sweating, either localized over the tumor or in the area of pain distribution, has been noted. Not infrequently glomus tumors erode bone, owing to the expansile character of the growth. When destruction of the cortex of a terminal phalanx is detected on x-ray examination, the presence of a subungual glomus tumor should be suspected.[11]

While pain is usually severe, a subcutaneous glomus tumor may not be visible. Love's † "pin test" may be a most valuable maneuver to localize it:

> An ordinary steel pin is used. The patient is asked to indicate the point of maximal pain or tenderness. Often, as the physician passes his finger toward the spot of maximal pain, the patient will withdraw the extremity, just as the patient with trigeminal neuralgia will withdraw his face when the trigger zones are approached. However, when the patient's confidence is gained, the point of a steel pin can be pressed into the skin as near as 1 cm. to the lesion without producing severe pain. As soon as the point is pressed over the lesion, the patient will have an attack of excruciating pain.

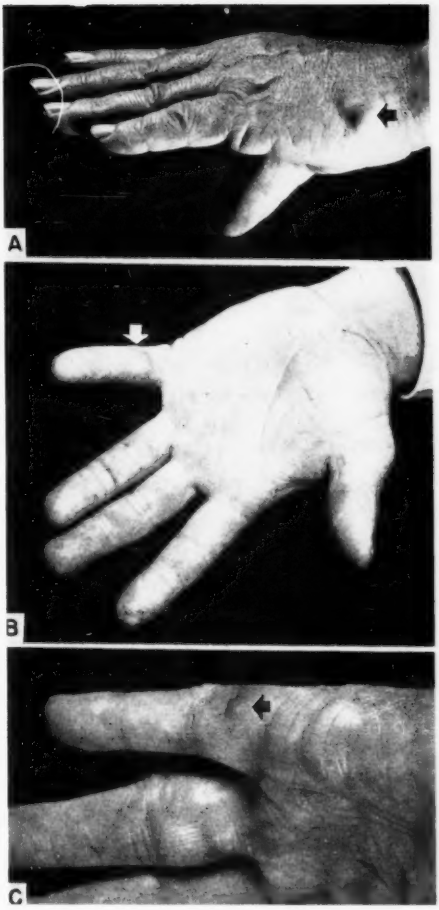

Fig. 1.—*A* and *B*, large glomus tumors; *C*, typical glomus tumor.

Because of the extreme tenderness manifested by these small nodules, most patients seek relief within a few months after onset of symptoms. However, a few instances are recorded of glomus tumors of 8 to 10 years' duration.

* References 6 and 7.

† References 14 and 15.

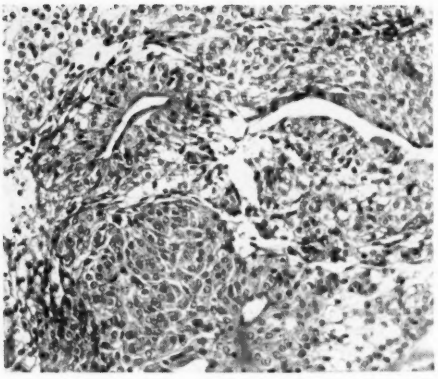

Fig. 2.—Glomus tumor (photomicrograph). There are many vascular lumina of varying sizes lined by a single layer of endothelial cells and surrounded by rows of typical glomal cells.

There is no known etiologic factor. Trauma has not been found to be significant.

MICROSCOPIC APPEARANCE

The microscopic picture of a glomus tumor resembles a normal glomus except for a decided increase in glomal cells and nonmyelinated nerve fibers. Microscopic examination reveals a tangled mass of endothelial-lined channels of various diameters, with walls composed of layers of glomal cells. The presence of large epithelioid glomal cells with myelinated and nonmyelinated nerve fibers in direct continuity with the cytoplasm is pathognomonic.

Glomus tumors have been recorded occasionally in deeper internal organs where the normal glomic structure is unknown. It is possible that an aberrant glomus may occur in various situations to account for these unexpected tumors; however, this is not likely. In 1942, Stout and Murray [12] reported an unusual type of vascular tumor which they called hemangiopericytoma. These tumors resemble closely the typical glomus tumor but have a more "organoid appearance." From tissue culture studies these authors produced evidence that the epithelioid cell of glomus tumors is similar and may be identical to the pericyte of Zimmermann, which is a smooth muscle cell found growing around capillaries. It may be postulated, therefore, that various types of tumors arise from the glomus, which is composed of vascular, epithelial, and nerve elements. It is possible that the so-called typical glomus tumor is a benign neoplasm representing the first tumor capability of the glomus, that the hemangiopericytoma is the next advanced tumor state of the glomus—capable of invasion and rarely of metastasis—, and that the final degree of tumor undifferentiation may be represented by various sarcomas originating in the mixed tissues of the glomic structure. This may also explain the occurrence of glomus tumors in sites where the normal glomic structure is not known.

DIFFERENTIAL DIAGNOSIS

Benign tumors of the skin, such as neuromas, lipomas, hemangiomas, and fibromas, may occasionally be confused with glomus tumors. Felon, subungual wart, subungual exostosis, or periostitis may produce symptoms characteristic of this tumor. Malignant skin tumors usually are differentiated by rate of growth and characteristic appearance. The appearance and symptoms of a glomus tumor are unique, and the correct diagnosis is not difficult, if the lesion is suspected.

TREATMENT

The glomus tumor is benign, and complete removal of the lesion by surgery is curative. Occasionally pain will persist in the immediate area for a few months postoperatively but will usually resolve without further treatment. Radiation, the injection of sclerosing agents, and periarterial sympathectomy are of no value.[13]

The microscopic appearance of each tumor should be carefully observed, and, if the diagnosis of hemangiopericytoma is established, a more extensive local excision is recommended, as invasion and metastases have been reported in such instances. It is apparently not possible to determine histologically a benign from a malignant hemangiopericytoma. Therefore, all tumors so diagnosed should be considered as local malignant growths and treated accordingly.

In the Table 25 cases from Duke Hospital covering the period from 1944 to 1954, inclusively, are reported and analyzed in order to substantiate the impression that although this tumor is not common, it is by no means a medical rarity.

Tumors of the Glomus

Case No.	Age, Yr.	Sex	Race	Diagnosis	Location
1	38	F	W	Glomus	Left middle finger
2	52	F	W	Hemangio-pericytoma	Left hand—hypothenar eminence
3	46	M	W	Glomus	Right heel
4	67	F	W	Glomus	Left lip
5	68	F	N	Hemangio-pericytoma	Back—right scapular area
6	34	F	W	Glomus	Right thumb
7	38	F	W	Glomus	Right index finger
8	48	M	N	Glomus	Right subungual
9	64	F	N	Glomus	Right neck
10	28	F	W	Glomus	Right index finger
11	51	F	W	Glomus	Sacrum
12	54	F	W	Glomus	Left knee
13	70	M	W	Glomus	Left hand—hypothenar eminence
14	18	M	W	Glomus	Left fifth finger
15	24	M	W	Hemangio-pericytoma	Sternum
16	62	M	W	Glomus	Left fifth finger
17	21	F	W	Glomus	Left index finger
18	38	F	W	Glomus	Right hand
19	64	F	W	Glomus	Lip
20	54	M	W	Glomus	Left ear
21	25	F	W	Glomus	Right thumb
22	48	F	W	Glomus	Right hand—thenar eminence
23	26	F	W	Glomus	Left index finger
24	24	M	W	Glomus	Right back
25	60	M	W	Glomus	Left leg

COMMENT

In the 25 presented cases, 16 patients were female and 9 male. Of the 16 female patients, 11 had glomus tumors of the extremities, thereby confirming the observation that women have a high percentage of these tumors on the extremities. However, six of the nine male patients had tumors of the extremities, showing also a predilection of this tumor for the extremities in men. It is interesting to note that in only one case was the tumor subungual, which is the site most usually regarded as typical.

The youngest patient recorded was 18 and the oldest 70 years of age. The age distribution was as follows: 18 to 30, seven patients; 30 to 40, four patients; 40 to 50, three patients; 50 to 60, four patients; 60 to 70, six patients; 70 and over, one patient. Except for the fact that apparently after puberty the glomus tumor can be encountered in any age group, we feel that no important correlation of age and tumor formation can be made from this small series. Three of our patients were Negroes; the remainder were white. These cases are presented to emphasize that the glomus tumor is not a rare medical condition, but instead it is a tumor which a busy practitioner can expect to encounter on numerous occasions throughout his medical career.

The proper treatment and care of such patients, therefore, should be familiar to the average physician, and particularly to the surgeon who diagnoses and treats lesions of the skin.

SUMMARY

A history of the glomus tumor is given. The anatomy and physiology of the normal glomus are reviewed and discussed. A description of the glomus tumor is presented, and the proper treatment of this lesion is suggested. Twenty-five cases of glomus tumors not previously reported are reviewed.

REFERENCES

1. Wood, W.: On Painful Subcutaneous Tubercle, Edinburgh M. & S. J. **8**:283, 1812.

2. Masson, P.: Le Glomus neuromyo-artériel des régions tactiles et ses tumeurs, Lyon chir. **21**:257-280 (May-June) 1924.

3. Mason, M. L., and Weil, A.: Tumor of Subcutaneous Glomus; Tumeur Glomique; Tumeur du Glomus Neuromyo-Artériel; Subcutaneous Painful Tubercule; Angiomyo-Neurome; Subcutaneous Glomal Tumor, Surg. Gynec. & Obst. **58**:807-816 (May) 1934.

4. Popoff, N. W.: Digital Vascular System: With Reference to the State of Glomus in Inflammation, Arteriosclerotic Gangrene, Diabetic Gangrene, Thromboangiitis Obliterans and Supernumerary Digits in Man, Arch. Path. **18**:295-330 (Sept.) 1934.

5. Lemmer, K. E.: Glomus Tumors: Summary of 15 Cases, Arch. Surg. **57**:531-538 (Oct.) 1948.

6. Eyster, W. H., Jr., and Montgomery, H.: Multiple Glomus Tumors, Arch. Dermat. & Syph. **62**:893-906 (Dec.) 1950.

7. Freedman, H.: Multiple Glomus Tumors, Brooklyn Hosp. J. **8**:4-13, 1950.

8. Jackson, H., and Balkin, R.: Glomus Tumors: Clinical and Pathologic Report of Unusual Case, Arch. Surg. **53**:100-104 (July) 1946.

9. Hopkins, G. S., and Olsen, A. K.: Subungual Glomus Tumor: Report of Case, Guthrie Clin. Bull. **18**:83-86 (Oct.) 1948.

10. Gold, H.: Glomus Tumours, Canad. M. A. J. **62**:64-67 (Jan.) 1950.

11. Mathis, W. H., Jr., and Schulz, M. D.: Roentgen Diagnosis of Glomus Tumors, Radiology **51**: 71-75 (July) 1948.

12. Stout, A. P., and Murray, M. R.: Hemangiopericytoma: Vascular Tumor Featuring Zimmermann's Pericytes, Ann. Surg. **116**:26-33 (July) 1942.

13. Martorell, F.: Glomus Tumors, Angiology **1**:451-456 (Dec.) 1950.

14. Love, J. G.: Glomus Tumors: Diagnosis and Treatment, Proc. Staff Meet. Mayo Clin. **19**:113-116 (March 8) 1944.

15. Love, J. G.: Glomus Tumors, Minnesota Med. **32**:275-277 (March) 1949.

CORRECTIONS

An ommission in the copy of the final paragraph of Dr. F. G. Kergins' discussion (p. 335) of the article "A Simplified and Rapid Anatomical Approach to Parotidectomy" by Drs. E. S. Brintnall, R. T. Tidrick, and W. C. Huffman, in the September, 1955, issue of the ARCHIVES, distorted the meaning of this paragraph. The paragraph should read as follows:

"Dr. Janes has maintained a follow-up over the past 20 years of these cases treated in the Toronto General Hospital, and he gives me these figures: There have been 32 patients operated on for carcinoma of the gland, and 89 benign tumors, none of which developed evidence of recurrence during the period of follow-up. I am afraid I don't have the figures for the carcinomas."

In the subtitle of the article, "Intravenous Cholecystography with a New Medium," by Dr. Theodore L. Orloff, on page 620 in the October issue, the generic name for Urokon Sodium was incorrectly spelled. This name thould be "sodium acetrizoate."

Thrombophlebitis of the Thoracoepigastric Vein

An Uncommon Benign Lesion of Undetermined Etiology

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The three case histories which follow are recorded for two reasons. The first is that the condition described is likely to cause unnecessary alarm in both patient and physician. It immediately suggests cancer, while, as a matter of fact, it is both benign and transient. The second reason is that almost nothing concerning this disease has appeared in the American literature and most of the physicians and surgeons with whom it has been discussed had never even heard of it.

REPORT OF CASES

CASE 1.—A 25-year-old white woman was seen Oct. 1, 1953, because a few days earlier, when she had attempted to turn on a light switch just out of reach, she became aware of a slightly painful area in the left inframammary region. She was inclined to attribute the discomfort to the vigorous water-skiing in which she had lately engaged. Physical examination was entirely negative except for a thin, string-like cord which could be palpated laterally from the region of the ninth left interspace, across the inframammary fold, and into the subcutaneous tissue of the left breast lateral to the nipple. This lesion, which was about 14 cm. long, was most readily palpated when the left arm was abducted and it was put on stretch; the cord was then particularly prominent in the region of the mammary fold. It was slightly tender along its whole length, but there was no redness or other evidence of infection, no associated mass or other lesion in the breast on either side, no discharge from the nipple, and no palpable axillary nodes. The tentative diagnosis was thrombosis of a superficial vein.

In spite of the absence of all other signs of malignant disease, biopsy of the breast was performed six days after the patient was first seen. The lesion so clearly present on the first examination had by now almost disappeared. The pathologic report was fibrofatty tissue with mild chronic inflammation.

No specific treatment was instituted. By the end of a month the cord had completely disappeared, and the slight tenderness which had brought the patient for examination disappeared soon afterward. There has been no recurrence of the trouble over a 16-month period of observation.

CASE 2.—A 45-year-old white woman was seen March 29, 1954, because the previous day, while bathing, she had noticed a cord-like mass beneath the right breast. It was slightly tender and slight pain was experienced when the right arm was moved. The patient had two explanations for the lesion: A day or two before it appeared she had hung up heavy winter clothing. Also, for the past three months she had been wearing a new style of brassière, with a tight band which fitted closely beneath the breasts and which left red marks on the skin, as she noticed when she removed the garment at night. As in the first case, physical examination was negative except for the presence of a thickened lesion, about the diameter of an ordinary piece of string (2 mm.), which extended from the right lateral thoracic wall, superficial to the ninth rib, to the subcutaneous tissues of the right breast approximately to the level of the nipple. The lesion was slightly tender, but, as in the first case, there were no other abnormalities.

Biopsy was recommended but was not urged when it was refused. The patient was merely told to procure a new style of brassière and to avoid heavy lifting and similar exertions. Three months later swimming still caused a slightly painful sensation in the affected area, but by this time the cord had become softer and more superficial. Shortly afterward it disappeared entirely, though slight tenderness persisted for a few weeks longer. There has been no recurrence in 10 months of observation.

CASE 3.—A 31-year-old white woman first noticed a small cord-like lesion beneath the left breast, over the seventh rib, Aug. 9, 1954. According to her husband, a physician, it was then 4 cm. long and 2 mm. in diameter and was very tender to

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pressure. Within a week it had extended, in the same cord-like form, to the upper outer quadrant of the left breast, about 4 cm. superior to the left nipple. Within the next three to four days it extended inferiorly to the left epigastric region and downward almost to the level of the umbilicus. There was no history of chills, fever, or any other abnormality. The patient attributed the lesion to a recent habit of reaching across a cabinet to turn on an electric fan, just out of reach. Examination revealed no abnormality other than the cord-like lesion described. It was slightly tender, and there was a reddish discoloration over the portion which lay under the skin of the breast. Abduction of the left arm made the cord more prominent in the inframammary region and produced a depression over the involved vein in the breast area lateral to the nipple.

In view of the experience in the two previous cases and the review of the literature which by this time had been undertaken, only observation was advised. At the end of a month the lesion was still present but was much less tender. At the end of 6 months it had disappeared, and the affected area was no longer tender.

COMMENT

The condition described in these three cases was apparently first recognized in 1922, by Fiessinger and Mathieu,[1] who recorded three cases. The most complete report to date is by Hughes,[2] who collected 34 cases reported in the literature up to 1949 and added 5 cases which he had observed himself. His collection does not include the six cases mentioned in the discussions of Mondor's * two reports. Mondor's own reports included 7 cases, but Leger,[5] in 1947, stated that he and Mondor had by that time observed 20. Additional cases recorded since Hughes' report include 10 by Sicard † (3 of his own, 6 reported to him by Kapitanoff, and 1 reported to him by Touzard and Darbon) and those by Küss ‡ and Lunn and Potter [8] (5). Sicard also mentioned a number of other cases recorded in the French literature but did not identify them. Whether the 26 cases described by Adair [9] in 1950 belong in this category seems somewhat doubtful, as will be pointed out shortly. Even if they are included, the total number of reported cases is probably not much more than 100, of which the great majority are in the French literature.

It is highly doubtful, of course, that all observed cases of this condition have been placed on record. The cases mentioned in the discussion of Mondor's papers,§ for instance, would apparently not have come to light without the stimulus of his reports. The illustrations which accompany this paper (Figs. 1 and 2), which were supplied to me by Dr. Walter G. Maddock,‖ concern a case which has not been reported.

It is curious, and at the same time typical, that when the first cases of an infrequent disease are encountered others are encountered shortly afterward. The three cases reported in this communication were observed in less than a year. Fiessinger and Mathieu [1] observed their three cases within a period of weeks and Kapitanoff commented to Küss ¶ that he had observed all seven of his cases in less than 2 years.

The nomenclature is still confused. The disease is usually called Mondor's disease, although, if the eponymic nomenclature is to be used, the honor should go to Fiessinger and Mathieu,[1] who reported their cases 17 years before Mondor wrote his first paper. These earlier observers used the term *thrombo-phlébites des vein de la paroi thoraco-abdominale*, a cumbersome name and not indicative of involvement of the specific blood vessel. Mondor,[3] when he reported his first cases, did not recognize the pathologic process as vascular and called the disease *tronculite sous-cutanée subaigüe de la paroi thoracique antéro-latérale*. When he reported his second series of cases [4] he recognized the disease as vascular and used the term *phlébite en cordon*. Hughes [2] used the term "sclerosing peri-angeitis of the lateral tho-

* References 3 and 4.

† In report of Kapitanoff.[6]

‡ In report of Kapitanoff.[7]

§ References 3 and 4.

‖ Personal communication to the author.

¶ In report of Kapitanoff.[7]

Fig. 1. — Thrombophlebitis of thoracoepigastric vein in woman 40 years of age (Courtesy of Dr. Walter G. Maddock).

racic wall," and Lunn and Potter [8] used the term "subcutaneous phlebitis of the breast region." Phlebitis of the thoracoepigastric vein seems a satisfactory term from the standpoint of both pathologic process and localization.

There is no longer any doubt that this is an inflammatory lesion. The earlier observers # all considered it a superficial thrombophlebitis, though they had no pathologic proof. Mondor,[3] who was at first undecided whether the lesion was lymphatic or venous, concluded, on the ground that there were no red blood cells in the biopsy tissue, that it was lymphatic. In a second biopsy specimen, however, he found conclusive proof of the vascular character of the lesion. A number of other observers have since then also identified the lesion as vascular. Lunn and Potter [8] concluded from the thinness of the muscle band and the paucity of elastic fibers in one of their three biopsy cases that the vessel in the specimen was a vein and not an artery. Hughes [2] regarded the essential lesion as a gross perivascular sclerosis.

Hughes [2] summarized the findings in nine biopsy "specimens obtained elsewhere" as

References 1, 10, 11, and 12.

Fig. 2.—Thrombophlebitis of thoracoepigastric vein demonstrated by infrared photography, which shows thrombotic area leading to major branch of veins of anterior chest wall (Courtesy of Dr. Walter G. Maddock).

follows: (1) the presence of one or more lumina; (2) thickening of the intima, which at times was almost complete; (3) gross thickening of the adventitia, either localized, with the appearance of grossly thickened vessels, or more diffuse and irregular; (4) predominant connective tissue proliferation with some smooth muscle tissue, and (5) wandering cells of both the small round and polymorphonuclear leucocyte type, with the proportion of each type varying from case to case. Hughes also stated that the total life history of the disease is 10 to 12 weeks and that the lesions can be graded according to their apparent histologic age.

Moschcowitz,[13] whose cases seem clinically identical with those reported by other observers, described epithelial tubules lined by flattened and columnar cells lying within a connective tissue matrix and surrounded in some areas by a considerable number of lymphocytes intermingled with occasional polymorphonuclear leucocytes and plasma cells. His suggestion that the condition is really a vestigial mastitis arising in a persistent milkline or milkridge, which is the earliest anlage of the breast, has not been well received.

The etiology of this special type of thrombophlebitis remains obscure. It has followed grippe, the removal of an inflamed axillary tumor, infection of the abdominal incision after an intestinal resection for diverticulitis, an operation for subacute appendicitis, and peritonsillar and apical abscesses. It seems highly doubtful, as Fiessinger and Mathieu [1] intimated in the first cases reported, that these preceding illnesses had anything to do with the development of the lesion.

Several cases were associated with anomalies of the breast * and with chronic bilateral mastitis.[2] Others were associated with carcinoma of the breast.† The specimens were negative for malignant disease in all cases in which biopsy specimens were taken. Almost all of Adair's [9] 26 cases, as already noted, followed surgery for mammary carcinoma. There was no evidence of malignant tissue in the lesions, and he attributed their development to too tight application of adhesive over the dressings, with resulting blockage of the return circulation of the superficial mammary veins to the axillary and subclavian veins. As Lunn and Potter [8] point out, it is possible for a breast support to impede the venous flow. One of my own patients attributed her lesion to a tight band on her brassière. From a number of aspects this seems reasonable theory, though it is by no means universally applicable.

Effort, trauma, and abrupt or straining movements were regarded as causative in a number of cases.‡ All three of my own patients were able to remember some special effort which preceded the appearance of the lesion, but in all three cases, as in most recorded in the literature, the story of trauma amounted to not much more than the story one could elicit from any patient engaged in his usual occupations and asked to recollect episodes of trauma.

All of these patients tell the same sort of story: Local pain or tenderness is experienced, the affected area is examined, and the lesion is found. Occasionally a mild ache presages its appearance. In some cases there is limitation of the upward motion of the arm on the affected side. Two of the patients of Daniels [10] complained that the pain was accentuated by deep breathing, and in one instance the similarity to fibrinous pleurisy was so strong that the chest was strapped.

Physical findings are scanty (Figs. 1 and 2). They are limited, in fact, to the appearance of a cord-like structure, 2 to 3 mm. thick, which usually takes its origin at the level of the umbilicus, just medial to the anterior axillary line, and extends directly upward across the subcostal margin. It may end lateral to the nipple, in the lower border of the pectoralis major muscle or may cross the submammary sulcus and end in the

* References 2 and 8.

† References 4, 6, and 8.

‡ References 3 and 12.

lower, outer quadrant of the breast. Even if it can be traced to the nipple, it still remains a dermal lesion, never extending to the deeper tissues. Usually the lesion is a single cord, but it may be accompanied by one or more similar cords, or, occasionally, may assume a plexiform pattern. In one of Hughes'[2] cases the cord bifurcated and the two branches continued downward 1 to 2 cm. apart to just above the costal margin. This lesion began at the level of the nipple and 5 cm. lateral to it. In another of Hughes' cases, when the breast was lifted three or four parallel ridges were seen extending vertically downward from the lower and outer quadrant to just beyond the costal margin.

The cord is usually tender and is occasionally hot or presents a reddish coloration. The covering skin may be elevated into a thin ridge or retracted into a groove. The appearance of the cord has been variously compared to that of a thin lead pencil, a knitting needle, a ureteral catheter, and an adult vas deferens. An occasional lesion is described as having a beaded appearance.

Usually the cord is evident when the affected area is inspected. In none of Daniels'[10] cases, however, was it visible. His opinion is that if palpation were routinely carried out when pain about the breast is complained of more cases of this disease might be diagnosed.

One hesitates to make dogmatic statements in connection with a lesion of the breast, in which cancer must always be thought of immediately and seriously. It is reasonable, therefore, when a physician first encounters phlebitis of the thoracoepigastric vein, for him to consider it neoplastic. It now seems safe to dismiss that idea. Even in the reported cases in which the condition was associated with mammary cancer, biopsy, whenever it was done, proved the involved vein to be free of disease. This form of thrombophlebitis does not seem to be an extension of mammary cancer, though, if there is any reason at all to suspect that malignant disease of the breast is present, no time must be lost in undertaking the usual diagnostic measures to confirm or exclude it. Otherwise, there seems no need for biopsy.

Spontaneous resolution, usually within a few months, has been the rule in all reported cases in which the end-result is mentioned, just as it was the end-result in the first three cases reported by Fiessinger and Mathieu[1] and in the three cases reported in this communication. Since the disease is apparently self-limited, no treatment other than observation is indicated. If the patient has been wearing a brassière with a tight band, which could conceivably cause venous obstruction, she should be advised to change to a more hygienic type of garment.

SUMMARY

Phlebitis of the thoracoepigastric vein is a cord-like lesion which on first inspection and examination suggests a malignant origin. The approximately 100 cases now on record in the literature do not support that point of view. Biopsy has been negative for cancer in all the cases in which it has been performed, and spontaneous resolution, within a matter of months, has occurred in all cases followed up sufficiently long to observe end-results. If, however, there is any reason at all to suspect that malignant disease may be present in the breast, the usual diagnostic measures should be resorted to at once. Three additional cases of this condition are recorded.

REFERENCES

1. Fiessinger, N., and Mathieu, P.: Thrombophlébites des veines de la paroi thoraco-abdominale, Bull. et mém. Soc. méd. hôp. Paris **36**:352-354 (Feb. 24) 1922.

2. Hughes, E. S. R.: Sclerosing Peri-Angeitis of the Lateral Thoracic Wall, Australian & New Zealand J. Surg. **21**:17-24 (Aug.) 1952.

3. Mondor, H.: Tronculite sous-cutanée subaigüe de la paroi thoracique antéro-latérale, Mém. Acad. chir. **65**:1271-1278 (Dec. 6) 1939.

4. Mondor, H.: Phlébite en cordon de la paroi thoracique, Mém. Acad. chir. **70**:96-98 (March 1) 1944.

5. Leger, L.: Phlébite en cordon de la antéro-latérale du thorax: Maladie de Mondor, Presse méd. **55**:849-851 (Dec. 20) 1947.

6. Kapitanoff, G.; Touzard, and Darbon: Maladie de Mondor, Mém. Acad. chir. **76**:939-945 (Dec. 13) 1950.

7. Kapitanoff, G.: Noveau case de maladie de Mondor, Mém. Acad. chir. **76**:945-947 (Dec. 13) 1950.

8. Lunn, G. M., and Potter, J. M.: Mondor's Disease (Subcutaneous Phlebitis of the Breast Region), Brit. M. J. **1**:1074-1076 (May 8) 1954.

9. Adair, F. E.: Cancer of the Breast, Practitioner **165**:473-481 (Nov.) 1950.

10. Daniels, W. B.: Superficial Thrombophlebitis: A New Cause of Chest Pain, Am. J. M. Sc. **83**:398-401 (March) 1932.

11. Williams, G. A.: Thoraco-Epigastric Phlebitis Producing Dyspnea, J. A. M. A. **96**:2196-2197 (June 27) 1931.

12. Robinson, R. H. O. B.: Thrombosis Following Strain, Brit. J. Surg. **23**:296-298 (Oct.) 1935.

13. Moschcowitz, A. V.: Vestigial Mastitis, a Hitherto Unrecognized Syndrome, Ann. Surg. **98**: 855-867 (Nov.) 1933.

Unusual Types of Interparietal Hernia

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It is well known that indirect inquinal hernias generally come through the internal inquinal ring, follow the inguinal canal downward, and emerge through the external inguinal ring, often becoming scrotal in character. The cases here reported did not follow that pattern at all. In the first case a huge hernia emerged through the internal ring and then pushed itself directly through the abdominal wall, including the aponeurosis of the external oblique muscle, and gave the appearance of being a ventral hernia. In the second case a strangulated hernia came through the internal ring, dissected upward between the internal and external oblique muscles but did not pierce the aponeurosis of the external oblique, as the first one did.

These hernias come in the category of interparietal hernias. Lower and Hicken [1] classify interparietal hernias anatomically as follows: "(1) Properitoneal hernia, that type in which the hernial sac lies between the peritoneum and the tranversalis fascia; (2) interstitial hernia, in which the sac lies between the transversalis fascia and the transversalis, internal oblique, or external oblique muscles; and (3) superficial hernia, in which the sac is situated between the aponeurosis of the external oblique muscle and the integument."

The first of these cases would have to be classified as the superficial type of interparietal hernia and the second as the interstitial type.

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It is generally assumed that interstitial hernias (the commonest type of interparietal hernia) are always inquinal hernias. This is not correct. One of us (A. R. K.) recently operated upon a case of incisional hernia in a McBurney scar, in which the hernia sac lay between the internal oblique muscle and the aponeurosis of the external oblique. Hernias in the linea semilunaris are also often of the same type and are masked by the fact that they do not come through the aponeurosis of the external oblique. This often makes the diagnosis difficult. One such case was recently reported by Larson.[2] His case involved the largest hernia in the linea semilunaris we have seen reported, the sac measuring 14×6 cm. It contained omentum and sigmoid, but the hernia contents were flattened out under the aponeurosis of the external oblique, concealing the nature of the condition, and the diagnosis was not made until operation.

REPORT OF CASES

CASE 1.—A 60-year-old white man was first seen by one of us (A. R. K.) on Feb. 12, 1951.

History.—The patient complained that his "stomach had fallen." He stated that the condition started 10 to 15 years previously and had got much worse during the last 4 or 5 years. It gave him no trouble unless he pressed on the offending spot, which was principally on the left side. There was no constipation, no nausea or vomiting, and no bleeding. He had always been overweight and had not weighed less than 250 lb. for many years.

Physical Examination.—The patient was a huge man, being 6 ft. tall and weighing 305 lb. There was a large hanging curtain of fat from the lower abdominal wall, much more pronounced on the left than on the right. There were striae on the skin, both on the right and on the left side, due to stretching. The external inguinal rings were slightly enlarged on each side, but there was no impulse on coughing. There was a mass about the size of a man's head in the left side of the hanging apron of fat. The mass was not reducible, and there was no impulse on coughing.

Impression.—Either a large lipoma or a ventral hernia with omentum in it.

Operation.—The patient was operated upon at the Union Memorial Hospital on March 1, 1951, under thiopental sodium (Pentothal Sodium), cyclopropane, and ether, with curare. A transverse elliptical incision was made across the entire abdomen, including the apron of fat, and the apron was excised. In doing this, the huge hernia sac was exposed and found to have a pedicle situated in the region of the left internal inguinal ring. The pedicle was 1½ in. in diameter. In coming into the subcutaneous position, the hernia sac had separated the fibers of the external oblique aponeurosis, and these were markedly atrophied. The spermatic cord was freed and found to enter the internal ring along with the neck of the hernia sac. However, there was no other connection between the cord and the hernia sac. The cord was retracted with a piece of gauze. The huge sac, which measured approximately 6×6×8 in., was opened and found to contain large loops of big bowel, which were greatly hypertrophied owing to their long domicile in this irreducible hernia sac. The hernia was of the sliding variety. It was impossible to reduce it by the usual methods. A LaRoque incision was therefore made, and, even by making traction from above and taxis from below, the mass of bowel could not be reduced into the abdominal cavity. An incision was then made in the linea semilunaris from the level of the internal ring to the level of the LaRoque incision, by a method previously described,[3] and a flap of the oblique muscles was reflected outward. The sac was dealt with by the LaRoque method.* Even with the large opening that had been made in the abdominal wall, the mass of bowel was reduced with great difficulty. After reduction, the intra-abdominal pressure was so great that it was difficult to keep the patient breathing. He had a short chest and a big belly, and the reduction of the mass of bowel increased the intra-abdominal pressure terrifically. The parietal peritoneum was closed with great difficulty with 0 nonabsorbable surgical (black silk) continuous sutures. There were some gaps in the closure, however, and these were closed by suturing muscle over them. The reflected flap of oblique muscles was then sutured back in place at the linea semilunaris with mattress sutures of 0 black silk. The La Roque incision was closed with interrupted nonabsorbable surgical sutures of 0 black silk. A Halsted[6] relaxation incision was then made in the sheath of the rectus muscle. Even with this incision there was still considerable tension. The conjoined tendon and transversalis fascia, which were not strong, were sutured to Poupart's ligament with interrupted sutures of 0 black silk. Several sutures were placed above the internal ring, snugly closing it around the cord. A piece of tantalum gauze approximately 6×2½ in. was then sutured over this first suture line, making a V-shaped slit for the cord at the internal ring.[7] The lower edge of the gauze was sutured to Poupart's ligament with interrupted sutures of medium black silk. The rest of the mesh was sutured to the muscles in various places, reinforcing them as much as possible. The external oblique aponeurosis was then sutured over the mesh, but throughout the upper three-fourths of the area the edges of the aponeurosis could not be approximated, because of tension. It was therefore sutured to the top of the mesh, the sutures going through the muscle under the mesh also. Toward the upper end of the area the mesh did not close the muscle defect completely; so another piece approximately 2½×2½ in. was sutured to the long anteromesial edge of the original piece of mesh. The cord was then dropped on the aponeurosis, being left in the subcutaneous position. No subcutaneous sutures were used, as the fat came together nicely without the necessity for any suturing. The huge skin incision was then closed with fine black silk continuous sutures. A cigaret drain was placed in the left end of the incision.

Postoperative Course.—Owing to the great increase in intra-abdominal pressure after reduction of the contents of the hernia sac, the patient had great difficulty in breathing and was kept on oxygen continuously administered through a mask for five days. After the continuous use of oxygen was discontinued, he had to have it intermittently for several days longer. He lost 25 lb. in weight while in the hospital and was discharged on the 16th postoperative day.

On March 28—four weeks after operation—the patient returned because he was having some discharge from the wound where the cigaret drain had been placed. A subcutaneous collection of fluid was found over the main operative site. This was aspirated and several hundred cubic centimeters of serosanguinous fluid removed. The patient was then readmitted to the Union Memorial Hospital. The next day an additional 400 cc. of the same type of fluid was aspirated. On April 1 there was no further pocked collection of fluid, but there was a good deal of drainage from the site of the cigaret drain. The wound was curetted through this drainage site with a long uterine curette, which went in up to the hilt, going across the abdomen subcutaneously. A great deal of granulomatous tissue was curetted out. The patient was discharged from the hospital the same day, and thereafter the wound healed perfectly without any further discharge.

He was last seen on April 11, 1955—over four years after his operation. The hernia site was firm. In spite of efforts to get him to reduce, he still weighed 260 lb.

* References 4 and 5.

CASE 2.—A 76-year-old white woman was first seen by one of us (E. S. S.) for a condition complained of on June 20, 1954.

History.—The patient developed a mass in the left lower abdominal quadrant in 1948. She did nothing about the mass until a few days prior to being seen, when she developed generalized abdominal pain. Two days before admission she took a laxative and developed diarrhea. After this she developed constipation and had no further bowel movement, although she did pass some gas the day before first being seen. Anorexia was present.

Physical Examination.—There was a mass about 4 in. in diameter in the left lower quadrant, which was hard and quite tender. The patient was nauseated but did not vomit. White-blood-cell count was 11,000, and hemoglobin was 10.2 gm.

Impression.—Those who saw the patient thought she might have an intraperitoneal abscess secondary to diverticulitis or a strangulated hernia as the cause of the obvious intestinal obstruction.

Operation.—The patient was operated upon at the Johns Hopkins Hospital on the day of admission (June 20, 1954), under thiopental sodium and nitrous oxide anesthesia. An oblique incision was made over the mass. The aponeurosis of the external oblique was split parallel to its fibers. When the aponeurosis had been divided, a larger hernial sac was exposed. This was opened, and it was found to contain several loops of small intestine and some cloudy fluid. The intestine was red and edematous in places, covered with fibrinous exudate, but the circulation was not impaired. The sac emerged from the internal ring, but, instead of going through the external ring, it had dissected upward between the internal and external oblique muscles. The contents of the sac could not be reduced until the fibers of the internal oblique and transversus had been divided. The bowel was replaced within the abdomen. The sac was dissected free, its neck ligated, and the remainder excised. The defect was repaired by approximating the conjoined tendon, internal oblique muscle, and transversalis fascia to the inguinal ligament. Interrupted 00 nonabsorbable surgical sutures were used. The aponeurosis of the external oblique was then imbricated over this, and the subcutaneous tissue and skin were then closed with interrupted sutures of 0000 silk.

On Sept. 24, 1954, there was no evidence of a recurrence.

COMMENT

It is believed that Case 1, a superficial type of interparietal hernia, would have been much better handled had the patient been given artificial pneumoperitoneum preoperatively [8] to enlarge his abdominal cavity. Had this been done, he would not have suffered the respiratory embarrassment he did suffer after reduction of the hernia contents. The hernia had almost, but not quite, forfeited the right of domicile. The reduction of the huge mass of bowel caused an unnecessary elevation of the diaphragm and consequent cardiac and respiratory embarrassment, which could have been avoided by the use of preoperative pneumoperitoneum.

Case 2 represents the interstitial type of interparietal hernia. While this is more frequently encountered than the superficial variety, as exemplified in Case 1, it is rare enough to be very uncommon and the diagnosis is often very difficult to make. Lower and Hicken stress the difficulty in preoperative diagnosis. This type of hernia is much rarer in the female than in the male, occurring three and a half times as frequently in men. It was first described by Bartholin, in 1661.[9] So far as we have been able to learn by a search of the literature, the first case of interstitial hernia described in a woman was that of Velpeau [10] in 1841. Luke [11] in 1850 reported two more cases. Golding-Bird [12] reported two cases in 1884, and Berger [13] three cases in 1891. In 1900 Auvray [14] reported a case and collected 13 others from the literature. One of us [15] recently reported a bilateral case (not strangulated) in a 25-year-old married woman.

SUMMARY

Two cases of interparietal hernia are here reported. The first case was a huge hernia of the superficial variety, which had almost forfeited the right of domicile and would have been better handled by giving the patient artificial pneumoperitoneum preoperatively. The second case was of the interstitial variety, was strangulated, and, owing to its anatomical peculiarity, made the preoperative diagnosis difficult.

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REFERENCES

1. Lower, W. E., and Hicken, N. F.: Interparietal Hernias, Ann. Surg. **94**:1070-1087 (Dec.) 1931.

2. Larson, E. E.: Spigelian Hernia, Am. J. Surg. **82**:103-106 (July) 1951.

3. Koontz, A. R.: The Operation for Difficult Sliding Hernia of the Large Bowel, Am. Surgeon **18**:78-84 (Jan.) 1952.

4. LaRoque, G. P.: The Intra-Abdominal Method of Removing Inguinal and Femoral Hernia, Arch. Surg. **24**:189-203 (Feb.) 1932.

5. Williams, C.: Repair of Sliding Inguinal Hernia Through the Abdominal (LaRoque) Approach, Ann. Surg. **126**:612-623 (Oct.) 1947.

6. Halsted, W. S.: Cure of the More Difficult as Well as the Simpler Inguinal Ruptures, Bull. Johns Hopkins Hosp. **14**:208-214 (Aug.) 1903.

7. Koontz, A. R.: The Use of Tantalum Mesh in Inguinal Hernia Repair, Surg. Gynec. & Obst. **92**:101-104 (Jan.) 1951.

8. Koontz, A. R., and Graves, J. W.: Preoperative Pneumoperitoneum as an Aid in the Handling of Gigantic Hernias, Ann. Surg. **140**:759-762 (Nov.) 1954.

9. Watson, L. F.: Hernia: Anatomy, Etiology, Symptoms, Diagnosis, Differential Diagnosis, Prognosis and Treatment, Ed. 3, St. Louis, C. V. Mosby Company, 1948, p. 154.

10. Velpeau, M.: Hernie inguinale étranglée de nouvelle espèce, chez une femme: Operation; Mort; Autopsie, Gaz. Hôp. **5**:2-4 (Jan. 5) 1841.

11. Luke, J.: Cases of Ascending or Intermuscular Hernia, with Observations, London M. Gazette **10**:458-461 (March 15) 1850.

12. Golding-Bird, C. H.: Two Cases of "Hernie en Bissac" in Women, One Being Also "Intraparietal," Tr. Clin. Soc. London **17**:210-213 (May 23) 1884.

13. Berger, P.: Sur quelques variétés de la hernie inguinale congénitale chez la femme; en particulier, des hernies compliquées d'un kyste du canal de Nuck et des hernies en bissac, Bull. et mém. Soc. chir. Paris **17**:283-294 (April 15) 1891.

14. Auvray, M.: Hernie inguino-interstitielle chez la femme (hernie de Goyrand), Gaz. hebd. méd. **5**:542-547 (June 10) 1900.

15. Koontz, A. R.: Interstitial Hernia: A Problem in Diagnosis, Postgrad. Med., to be published.

Experimental Studies on the Secretions of the Isolated Duodenum

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There has long been an interest in the role played by the duodenum in gastrointestinal physiology. Numerous reports have appeared describing the secretions of the duodenum and the regulatory role played by the duodenum in the control of secretions from the stomach, gall bladder, and pancreas. However, much that is known about duodenal physiology has been learned indirectly by intubation of patients or animals and by the study of isolated short segments of duodenum. These methods, while they have been productive of much valuable information, have severe limitations. Though Walters and Bollman [1] succeeded in completely isolating the duodenum, they made no attempt to study the secretion quantitatively.

In this laboratory methods have been developed for the quantitative collection of gastric juice from dogs. With modern operative techniques, as well as a better understanding of fluid and electrolyte balance, it has been possible to prepare many types of gastric pouch animals and to maintain dogs who have continual marked electrolyte and fluid loss for long periods of time. It was thought possible to apply these methods to the study of the duodenum, and, consequently, a method has been devised for isolating the entire duodenum and collecting its secretion quantitatively. It is the purpose of this report to describe the operative technique used by us, to present data concerning the quantitative and qualitative description of the secretion of the duodenal mucosa, and to examine the effect of various substances on this secretion.

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OPERATIVE TECHNIQUE

Mongrel dogs weighing from 12 to 28 kg. were operated on under ether anesthesia after induction with thiopental sodium. The abdomen was entered through a midline incision, and the hepatoduodenal ligament was severed. The pylorus was transected and the distal end infolded in three of the dogs. In the remaining two, a method similar to that of Wright and co-workers [2] was used, in an attempt to preserve vagal innervation to the duodenum. A longitudinal incision was made near the greater curvature, extending from 1 to 2 cm. on either side of the pylorus. Through this incision, the mucosa over the pyloric muscle was undermined and transected transversely. Both ends of mucosa were infolded, and the longitudinal incision was closed, leaving an intact seromuscular bridge connecting the gastric antrum to the first portion of the duodenum but effectively blocking the pylorus so that food could no longer enter the duodenum.

The common bile duct was then severed between ligatures, as was the accessory pancreatic duct, which in the dog enters the duodenum in close proximity to the common duct. The main pancreatic duct was isolated, and the distal end was cut out of the duodenum along with a small button of duodenal wall surrounding it. The small bowel was severed in the region of the duodenal-jejunal junction, and the proximal end was infolded after a Stainless Steel cannula was placed near the distal end of the duodenum. The reentry of bile and pancreatic juice into the small bowel was accomplished in either one of two different ways. In some dogs the ligament of Treitz was severed so that the jejunum could be mobilized. The end of the jejunum was anastomosed in one layer to the gall bladder after a 1 to 2 cm. incision was made in the gall bladder. The pancreatic duct was then anasto-

mosed to a portion of jejunum just distal to this, and a gastroenterostomy was accomplished shortly beyond this point. In other animals the cut end of the jejunum was infolded and the first portion of the jejunum was left in its anatomical position, held in place by the ligament of Treitz. A loop of proximal jejunum was pulled up into the right upper quadrant, and the pancreatic duct was anastomosed to the ascending portion of the loop. The cholecystojejunostomy was done at the apex of the jejunal loop, and the gastroenterostomy was done so that the stomach emptied into the descending portion of the loop of jejunum. It was believed that the bile and pancreatic juice should enter the jejunum proximal to the gastrojejunostomy, in order to protect the dogs from gastrojejunal ulceration.

duodenum, a longitudinal incision of about 2.5 cm. was made near the greater curvature just proximal to the pylorus for the gastrojejunal stoma.

The cannula was brought to the outside through a stab wound in the abdominal wall after it was carefully wrapped with omentum. The abdominal incision was closed in two layers. A diagram of one of the resulting preparations can be seen in Figure 1. In some animals the operation was done in two stages, but it was found that it could be done relatively easily in one stage, and the majority of animals tolerated the procedure well.

POSTOPERATIVE TREATMENT

Early in our experience with this preparation, the mortality in the first few post-

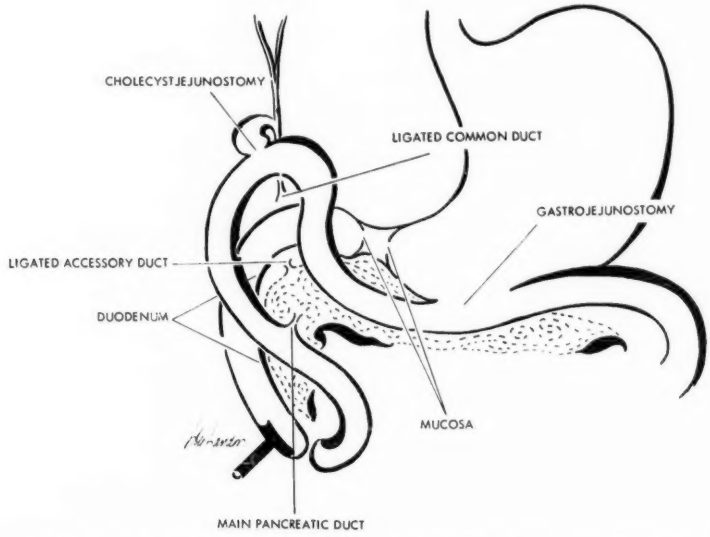

Fig. 1.—Diagram of one of the preparations used in this experiment. The mucosa is infolded on either side of the pylorus, but the seromuscular layer remains intact.

The pancreaticojejunal anastomoses were accomplished by pulling the button of duodenal wall left attached to the end of the pancreatic duct into a stab wound in the jejunum by means of sutures which were later tied on the outside of the jejunum, thus holding the duct in place within the lumen of the jejunum. The portion of the pancreas immediately surrounding the duct was tacked against the jejunum with interrupted sutures, in order to seal off the entrance of the pancreatic duct. In those dogs in which the pylorus was transected, the pyloric muscle was resected and the distal end of the gastric antrum was used for the gastroenterostomy. In the dogs which had an intact seromuscular bridge connecting the stomach to the

operative days was 100%, and autopsy of these animals failed to disclose pathological changes of a nature serious enough to account for the deaths. It had been shown by Dragstedt and co-workers [3] and later by Mann and Kawamura [4] that dogs could survive complete extirpation of the duodenum and that, therefore, the earlier ideas that the duodenum was as necessary to life as the adrenals or parathyroids were false. It seemed to us that isolation of the duodenum should be feasible, despite the fact that Matthews [5]

stated as late as 1939 that duodenal juice is necessary to life.

Reevaluation of the problem revealed that the dogs secreted large volumes of juice immediately after operation, some animals secreting as much as 1500 cc. in a single 24-hour period. It had been our practice to replace this fluid by parenteral administration of isotonic saline and Ringer's solution. It occurred to us that, if the dogs were losing potassium in the duodenal secretion, the deaths could very likely be due to hypokalemia. Consequently, we began adding 1.0 to 2.0 gm. of potassium chloride to the parenteral fluids each day and have since had no difficulty in maintaining the dogs until they are able to eat, in three to six days.

In view of the earlier ideas about the necessity of duodenal juice to life, further study of the electrolyte balance in the immediate postoperative period was undertaken. The duodenal juice was analyzed on many occasions for its electrolyte content. It was found to contain 5.3 to 9.3 mEq. of potassium per liter, 138 to 156 mEq. of sodium per liter, and 103 to 139 mEq. of chloride per liter. Assuming a secretion of 1500 cc. in 24 hours, one can see that the potassium loss could be as great as 14 mEq. per day. In terms of KCl, this would equal 1044 mg. of the salt. Dogs who received 1500 to 2000 cc. of isotonic saline per day with 1.0 to 2.0 gm. of KCl added maintained completely normal serum electrolytes throughout the postoperative period.

In order to determine that the success of this management was due to replacement of potassium rather than to the greater facility with which the operation was accomplished after we had gained experience with it, a dog was provided with an isolated duodenum and was given no potassium in the postoperative period. This animal, D-28, received 500 cc. of isotonic saline immediately after operation and 500 cc. of isotonic saline twice daily after this. The duodenal secretions were collected and measured every morning at 8 o'clock, at which time blood was drawn for electrolyte determinations. The course is depicted in Figure 2.

As can be seen, there is a steady rise in the serum sodium and chloride. As was expected, the serum potassium started to decline after the second postoperative day.

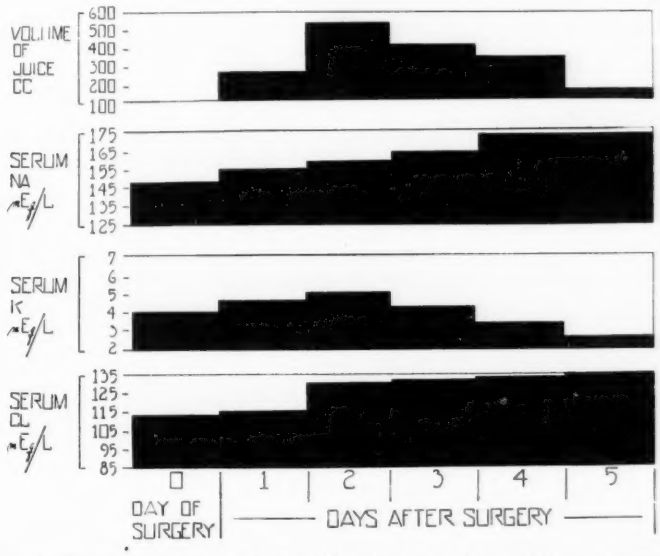

Fig. 2.—Postoperative course of D-28. This animal was given 1000 cc. of normal saline each day with no potassium in the fluids. It was found dead on the morning of the sixth day.

On the sixth postoperative day, the dog showed signs of weakness and lassitude and died that night. Its serum potassium on the last morning of life was 2.7 mEq/Liter. There were no pathological findings at autopsy except for patches of pneumonitis, such as are always found terminally in debilitated dogs.

Because it was felt that the giving of saline probably increased the rate of duodenal secretion and brought about a "washing out" of potassium in the duodenal juice, another dog, D-19, was provided with an isolated duodenum and given no parenteral fluid after operation. This dog was allowed to drink water ad lib but, despite obviously severe dehydration, did not drink more than a few hundred cubic centimeters of water each day. His secretions were collected and measured each morning, and blood was drawn for electrolyte determinations as in the previous animal. The results are depicted in Figure 3.

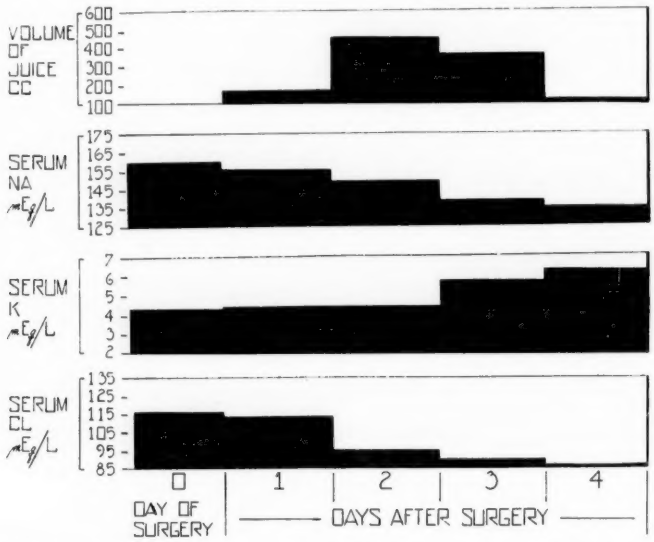

Fig. 3.—Postoperative course of D-19. This animal was given water per os and no parenteral fluids during the period shown. Food with salt added was given after the fourth day, and the dog made a satisfactory recovery.

The serum sodium and chloride in this animal showed a gradual decline, whereas the serum potassium showed a gradual slight increase. The amount of secretion from the isolated duodenum was considerably less than in the dog which had been given parenteral fluids. After four days it became clear that the dog was certainly not going to die of hypokalemia. He was allowed to eat the regular kennel diet with salt added and quickly regained strength and recovered from the operation.

The hypersecretion which was regularly found in the immediate postoperative period in dogs who were kept well-hydrated was very striking. In each dog the amount of juice secreted every 24 hours showed a gradual decline each day until it became stable at the end of one to two weeks. This decline in volume invariably occurred, even if the animal continued to receive 1500 to 2000 cc. of parenteral fluids each day. The hypersecretion appears to be a curious phenomenon associated with the initial isolation of the duodenum, for it has never reappeared when the dogs were subjected to subsequent operation and placed on parenteral fluids for a few days.

EXPERIMENTAL METHODS AND RESULTS

The juice from the duodenum was collected in rubber football bladders attached to the Stainless Steel cannulae. The bags were changed once or twice daily, and the secretion was carefully measured. The dogs were fed a standard diet of horse meat, Pard, bread, and milk, supplemented with approximately 5 gm. of sodium chloride a day, and on this regimen were able to maintain or gain weight and stay in electrolyte balance. Two of the dogs, D-884 and D-891, were given no added salt in their diet for a period of three weeks, and their serum electrolytes were followed during this time. Though no consistent changes from the normal occurred, D-891 showed a serum chloride of 88 mEq. per liter at the end of the three-week period, and it was thought best to give added salt to the animals as a precautionary measure.

TABLE 1.—*Average Twenty-Four-Hour Volumes and pH's of Duodenal Secretions Collected over a Thirty-Day Period After the Animals Had Been Stabilized*

	Volume		pH	pH Range
	Cc.	Range		
D-884	267	170 to 380	6.73	6.50 to 6.90
D-885	291	175 to 490	6.77	6.57 to 7.18
D-891	226	175 to 400	7.02	6.70 to 7.43
D-964	196	150 to 260	7.15	6.85 to 7.37
D-970	662	450 to 920	6.98	6.80 to 7.05

Within a week or two after the operation the character of the juice gradually changed from clear and watery to turbid and foul-smelling. Microscopic examination of the sediment revealed cellular debris and myriads of bacteria, chiefly Gram-negative rods. Attempts to keep the duodenum from becoming infected by sterilizing the rubber football bladders were unsuccessful, but the infection could be brought under control by administration of one of the broad-spectrum antibiotics. This did not have any appreciable affect on the quantity of juice secreted.

Table 1 gives the average volumes of juice secreted daily over a 30-day period by the five dogs included in this presentation. The average 24-hour collections over the 30-day period are as follows: D-884, 267 cc.; D-885, 291 cc.; D-891, 226 cc.; D-964, 196 cc., and D-970, 662 cc. Differences in volume are most likely due to variation in the length of duodenum utilized and in the size of the animals.

In Table 1 can also be found the average pH's of the juice of the five animals during the same 30-day period. The average pH's for these dogs during this period are as follows: D-884, 6.73; D-885, 6.77; D-891, 7.02; D-964, 7.15, and D-970, 6.98. These are not as alkaline as the juice collected by Florey and Harding [6] or by Wright and coworkers,[2] who found pH's ranging from 8 to 9. However, their collections were made from small segments which were presumed to include only the area of Brunner's glands. Since the juice collected in these experiments contained the secretions from both the area of Brunner's glands and the rest of the duodenal mucosa, it is apparent that the juice from the duodenal mucosa is lower in pH than that of the Brunner's glands. In general, the dogs whose secretion had a higher pH were those animals with relatively shorter segments of isolated duodenum, so that the secretion from Brunner's glands formed a higher proportion of the total secretion in these animals.

The duodenal juice was analyzed for trypsin by Anson's method [7] and for amylase and lipase.[8] Trypsin was found to be present only in juice from dogs who had not had the accessory pancreatic duct ligated during the first operation. When this duct was successfully ligated, no trypsin was found in the juice of any of the dogs when tested on several occasions. In one dog, D-891, in which it was thought that the accessory duct had been ligated during the initial procedure, trypsin was found in the juice. The dog ate poorly and did not do well. At reexploration an accessory pancreatic duct was found between ligatures. All traces of trypsin disappeared from the juice immediately, the amount of lipase decreased markedly, and the dog began to eat better and has since gained weight.

Both lipase and amylase were consistently found in the duodenal juice. These findings are borne out by the work of Wright and associates,[2] who found amylase and a trace of lipase but no protease or peptidase in the secretion from the first portion of the duodenum. However, Florey and Harding [9] were unable to find amylase or lipase in the juice collected from similar preparations. Some of the juice from our dogs was tested for saccharase and lactase, and these enzymes were also found to be present.

Effects of Histamine.—Koskowski [10] stated that subcutaneous administration of histamine in dogs caused secretion from an intestinal Thirty-Vella fistula. Nechoroschew [11] and Cajori [12] also found an increase in intestinal secretion in dogs after the parenteral administration of histamine. However, Lim and co-workers [13] could find no evidence that histamine stimulated the production of juice from the human duodenum. Florey and Harding [9] and Wright and associates [2] concluded that histamine did not stimulate the area of Brunner's glands in the duodenum in decerebrate cats.

In the present series of experiments, the dogs were fasted for at least 18 hours. At the end of this time, the secretion was collected every 20 minutes for one hour to establish the control level of secretion. Histamine acid phosphate was then administered subcutaneously, and the secretion was collected every 20 minutes for two hours after this. Several doses of histamine were used. When 0.55 mg. histamine acid phosphate (containing 0.2 mg. histamine base) or 1.10 mg. histamine acid phosphate was used, there was no effect on the rate of secretion of the isolated duodenums. However, when 2.75 mg. of histamine acid phosphate was given, there was usually an increase in secretion during the first 20 minute period after injection. The increase never amounted to more than a few cubic centimeters and, after their initial increase, the secretion returned to the control level or, in some cases, even lower. Some representative experiments in which the largest dose of histamine used was given are shown in Table 2.

Effects of Secretin.—Florey and Harding,[14] using short segments of duodenum isolated between the pylorus and the common bile duct in cats, found that intravenous injection of crude secretin or purified secretin (Mellanby's method) caused these segments to secrete. In addition, they found that the same type of food which caused the pancreas to secrete also caused the area of Brunner's glands to secrete, and in the same short latent period. From this data they concluded that Brunner's glands in the cat are controlled by secretin. Fogelson and Bachrach [15] also found that vasodilatin-free secretin caused the area of Brunner's glands to secrete and that the height of the secretory curve coincided with increased motility of the duodenum. Wright and co-workers [2] found that intravenous administration of secretin increased the secretion from transplanted segments of duodenum in cats.

On the other hand, Sonnenschein and Ivy [16] and Sonnenschein, Grossman, and Ivy [17] found that in dogs no significant response to crystalline secretin was obtained from pouches made from the first portion of

TABLE 2.—*Effect of Histamine on the Volume of Juice Secreted by the Duodenum in Fasting Dogs*

	Volume of Duodenal Secretions, Cc.								
	Before Injection of Histamine Acid Phosphate			After Subcutaneous Injection of 2.75 Mg. of Histamine Acid Phosphate					
Dog	At 20 Min.	At 40 Min.	At 60 Min.	At 20 Min.	At 40 Min.	At 60 Min.	At 80 Min.	At 100 Min.	At 120 Min.
D-884	2.0	1.0	2.0	8.0	3.0	2.5	2.0	3.5	2.5
D-885	4.0	2.5	3.0	6.0	1.5	1.5	2.5	1.5	3.0
D-891	2.5	2.5	2.0	6.0	2.0	2.0	2.5	3.0	2.5
D-964	6.0	4.5	2.0	7.0	3.0	4.0	2.0	3.5	3.5
D-970	5.0	5.0	4.5	13.0	3.0	4.0	3.5	5.0	5.0

the duodenum, some of which were transplanted subcutaneously. However, injection of a crude extract of intestinal mucosa (SI) containing secretin brought about an increase in duodenal secretion. Injection of a solution of SI rendered secretin-free by aniline precipitation [16] also evoked a secretory response from the isolated segments. Blickenstaff, Grossman, and Ivy [18] also confirmed the fact that SI causes the duodenal mucosa to secrete and that this could occur independently of motility, since flaps of duodenal wall sutured to the outer abdominal wall secreted in response to SI.

In our experiments a solution of pure secretin * was used. After the dogs were fasted for at least 18 hours, their secretion was collected every 20 minutes for 1 hour. Following the intravenous injection of 50 clinical units of secretin, the secretions were collected every 20 minutes for 2 hours. The experiment was repeated on another day with 100 clinical units of secretin. In no case was there a significant change in the rate of secretion above the basal rate. The results of a representative experiment are presented in Table 3.

TABLE 3.—*Effect of Secretin on the Volumes of Juice Secreted by the Duodenum in Fasting Dogs*

	Volume of Duodenal Secretions, Cc.								
	Before Injection of Secretin			After Intravenous Injection of 100 Clinical Units of Secretin					
Dog	At 20 Min.	At 40 Min.	At 60 Min.	At 20 Min.	At 40 Min.	At 60 Min.	At 80 Min.	At 100 Min.	At 120 Min.
D-884	5	3	2	4	2	2	2	2	2
D-885	5	5	5	10	5	3	5	5	3
D-891	6	5	2	3	3	3	4	4	5
D-904	4	4	3	7	3	3	3	4	3
D-970	15	11	12	15	8	8	8	10	15

Attempts to Demonstrate Vagal Control of Duodenal Secretion.—Florey and Harding [19] found that in cats and rabbits the secretion of isolated segments of the duodenum containing the area of Brunner's glands was unchanged by vagotomy. Furthermore, segments which had been transplanted subcutaneously and, subsequently, severed from their original blood and nerve supply continued to react in the normal way, secreting only when the animal was fed. The same authors [14] could find no evidence that the secretion from the area of Brunner's glands was affected by the sight or smell of food. However, Wright and co-workers [2] using decerebrate cats, found that electrical stimulation of the vagi in the chest caused a prompt secretion from the duodenal mucosa. They state further that the secretion from the area of Brunner's glands was more profuse than that from the rest of the duodenum. Histologically, stimulation of the vagi caused exhaustion of Brunner's glands.

We have used the gastric secretory response to insulin hypoglycemia for many years to determine whether gastric pouches in animals are vagally innervated and to establish the completeness of vagotomy in human patients. We are confident that insulin hypoglycemia is an adequate stimulus to excite the vagus centers and to cause the vagally innervated gastric glands to secrete. With this in mind we decided to test the effect of insulin hypoglycemia on the secretion from the duodenum in an attempt to see if vagal control of duodenal secretion could be demonstrated by this method.

The animals were again fasted for approximately 18 hours, and their control secretions were collected every 20 minutes for one hour. After this, 10 units of crystalline insulin were given intravenously, and the secretions were then collected every 20 minutes for two hours. In our experience the peak of gastric secretion from a normally innervated stomach occurs from 30 to 90 minutes after the intravenous administration of the insulin. However, none of the dogs showed a response during the two hours following insulin injec-

* Eli Lilly & Company, CT-446.

TABLE 4.—*Effect of Insulin Hypoglycemia on the Volume of Juice Secreted by the Duodenum in Fasting Dogs*

	Volume of Duodenal Secretions, Cc.								
	Before Insulin Injection			After Intravenous Injection of 10 Units of Insulin					
Dog	At 20 Min.	At 40 Min.	At 60 Min.	At 20 Min.	At 40 Min.	At 60 Min.	At 80 Min.	At 100 Min.	At 120 Min.
D-884	3	4	4	3	5	5	2	3	3
D-885	5	4	4	4	10	3	3	3	4
D-891	2	3	2	4	3	3	2	2	2
D-964	4	3	3	3	3	1	2	2	3
D-970	4	6	4	2	2	2	2	2	2

tion which could be interpreted as a significant increase over the basal level of duodenal secretion. The two dogs (D-964 and D-970) in which a careful attempt was made to preserve vagal innervation to the duodenum show only the random variations in secretion which were typical of all the dogs during successive 20-minute collections. The results of a typical experiment can be seen in Table 4.

Effect of Food.—Food was found to be an adequate stimulus for secretion from isolated segments of the first portion of the duodenum by Wright and associates,[2] Florey and Harding,† Sonnenschein, Grossman, and Ivy,[17] and Blickenstaff, Grossman, and Ivy.[18] In addition, Sonnenschein and Ivy[16] and Sonnenschein, Grossman, and Ivy[17] found that similar pouches, when denervated by subcutaneous transplantation and subsequent severing of the vascular pedicle, also responded to feeding.

To test the effect of feeding on the duodenal secretion, the animals were fasted for approximately 42 hours. Their secretion was then collected during the next hour. After this, they were fed a meal composed of a mixture of horse meat, bread, and Pard and any uneaten portion was taken away at the end of one hour. The duodenal secretions were collected every hour for 12 hours, and the volumes were carefully measured. Hourly collections were then stopped, and the total secretion for the next 12 hours was collected and measured. The results are given in Table 5.

As can be seen from the volumes secreted during the hour before feeding, prolonged fasting does not depress duodenal secretion to very low levels. After the meal there is no marked secretory response. Most of the dogs continued to secrete at a rate not significantly different from the fasting rate. The two dogs in which the vagal innervation to the duodenum is, presumably, intact (D-964 and D-970) show no immediate increase in secretion which could be interpreted as a counterpart to the psychic phase of gastric secretion. Four out of the five animals secreted more during the first 12 hours than during the second 12 hours, but the differences are not at all striking. The results indicate that there is little, if any, effect of feeding on the duodenal secretion when food does not come in contact with the duodenal mucosa.

† References 9, 14, and 19.

TABLE 5.—*Effect of Food on the Secretions of the Duodenum in Dogs*

	Volume of Duodenal Secretions, Cc.														
	Hourly Volumes After a Normal Meal (Uneaten Food Removed at End of First Hour)														
Dog	After Fasting 1 Hour	1	2	3	4	5	6	7	8	9	10	11	12	First 12 Hours	Second 12 Hours
D-884	7	16	11	13	7	6	6	11	8	11	10	12	4	115	80
D-885	12	14	7	8	10	7	12	13	7	16	15	15	5	129	150
D-891	10	9	10	10	15	10	11	13	7	14	7	4	4	114	92
D-964	7	5	4	4	5	5	7	4	12	5	4	5	7	67	60
D-970	14	10	14	13	13	14	17	23	16	21	15	10	13	179	94

COMMENT

The relatively large quantity of juice secreted by these animals during a 24-hour period was rather surprising to us, especially the large volumes secreted in the immediate postoperative period. After a period of one to two weeks, the rate of secretion of the duodenal mucosa becomes relatively constant for a given dog. It is apparent that potassium must be added to the parenteral fluids given in the postoperative period if serious trouble from hypokalemia is to be avoided. The failures reported in the earlier literature, when attempts were made to construct duodenal fistulae, were very likely due to ignorance of the crucial importance of potassium replacement and of electrolyte and water balance in general. While it is possible for a dog to survive the operation with no parenteral fluid administration whatsoever, we believe that recovery is quicker and needless risks are avoided if the dogs are kept well hydrated and careful attention paid to their electrolyte balance.

It is also surprising that the secretion is not markedly affected by large doses of histamine and is not significantly changed by oral ingestion of food or by fasting. It should be pointed out again that the secretions measured by us include those of Brunner's glands as well as those secreted by the rest of the duodenal mucosa. Our results should not be interpreted as contradicting those of others who worked primarily with the small area of duodenum containing Brunner's glands. Since the secretion from Brunner's glands undoubtedly represented a very small portion of the secretion collected by us, it is entirely possible that the substances used in attempts to stimulate secretion have an effect on the area of Brunner's glands which is masked by the relatively large basal secretion from the rest of the duodenal mucosa.

SUMMARY

A method is described for isolating the denal secretion, uncontaminated with bile or entire duodenum in dogs so that the duopancreatic juice, can be collected quantitatively.

The problem of electrolyte balance, with particular reference to potassium, in the immediate postoperative period is discussed.

The duodenal secretions contain amylase, lipase, saccharase, and lactase.

Histamine has a slight but transient stimulatory effect on the secretion of the isolated duodenum.

Secretin had no demonstrable effect on the rate of secretion of the isolated duodenum.

No evidence for vagal control of duodenal secretion could be found when the vagi were stimulated by insulin hypoglycemia.

Feeding has no clear-cut effect on the secretions of the isolated duodenum.

Continued loss of the duodenal secretions does not produce as severe demineralization and dehydration as occurs after loss of gastric or pancreatic juice. Death with very low concentration of serum potassium may take place within a few days of establishment of the fistula.

REFERENCES

1. Walters, W., and Bollman, J. L.: The Toxemia of Duodenal Fistula: Physiological Changes Concerned in the Production of Its Characteristic Chemical Reaction of the Blood, J. A. M. A. **89:** 1847-1853, 1927.

2. Wright, R. D.; Jennings, M. A.; Florey, H. W., and Lium, R.: The Influence of Nerves and Drugs on Secretion by the Small Intestine and an Investigation of the Enzymes in Intestinal Juice, Quart. J. Exper. Physiol. **30:**73-120, 1940.

3. Dragstedt, L. R.; Dragstedt, C. A.; McClintock, J. T., and Chase, C. S.: Extirpation of the Duodenum, Am. J. Physiol. **46:**584-590, 1918.

4. Mann, F. C., and Kawamura, K.: An Experimental Study of the Effects of Duodenectomy, J. A. M. A. **73:**878-880, 1919.

5. Matthews, A. P.: Physiological Chemistry, Ed. 6, Baltimore, Williams & Wilkins Company, 1939, p. 627.

6. Florey, H. W., and Harding, H. E.: The Function of Brunner's Glands and the Pyloric End of the Stomach, J. Path. & Bact. **37:**431-453, 1933.

7. Anson, M. L.: The Estimation of Pepsin, Trypsin, Papain, and Cathepsin with Hemoglobin, J. Gen. Physiol. **22:**79-89, 1938.

8. Koch, F. C., and Hanke, M. E.: Practical Methods in Biochemistry, Baltimore, Williams & Wilkins Company, 1953, p. 152.

9. Florey, H. W., and Harding, H. E.: Further Observations on the Secretion of Brunner's Glands, J. Path. & Bact. **39**:255-276, 1934.

10. Koskowski, W.: The Influence of Histamine on the Intestinal Secretion of the Dog, J. Pharmacol. & Exper. Therap. **26**:413-419, 1926.

11. Nechoroschew, N. P.: Histamin und periodische Tätigkeit des Verdauungskanals, Ztschr. ges. exper. Med. **66**:728-733, 1929.

12. Cajori, F. A.: The Enzyme Activity of Dogs' Intestinal Juice and Its Relation to Intestinal Digestion, Am. J. Physiol. **104**:659-668, 1933.

13. Lim, R. K. S.; Matheson, A. R., and Schlapp, W.: Observations on the Human Gastroduodenal Secretion with Special Reference to the Action of Histamine, Quart. J. Exper. Physiol. **3**:361-391, 1922-1923.

14. Florey, H. W., and Harding, H. E.: The Nature of the Hormones Controlling Brunner's Glands, Quart. J. Exper. Physiol. **25**:329-339, 1935.

15. Fogelson, S. J., and Bachrach, W. H.: Response of Brunner's Glands to Secretin, Am. J. Physiol. **128**:121-123, 1939.

16. Sonnenschein, R. R., and Ivy, A. C.: Humoral Control of Brunner's Glands, Fed. Proc. **4**:66, 1945.

17. Sonnenschein, R. R.; Grossman, M. I., and Ivy, A. C.: The Humoral Regulation of Brunner's Glands, Acta med. scandinav., Supp. 196, pp. 296-307, 1947.

18. Blickenstaff, D.; Grossman, M. I., and Ivy, A. C.: Stimulating Effect of Sugar, Fat and Meat Meals on Duodenal Secretion in the Dog, Am. J. Physiol. **158**:122-128, 1949.

19. Florey, H. W., and Harding, H. E.: A Humoral Control of the Secretion of Brunner's Glands, Proc. Roy. Soc., London, s. B, **117**:68-77, 1935.

Management of Adrenocortical Insufficiency During Surgery

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Adrenocortical insufficiency, known to be present in patients with Addison's disease and in patients who have had bilateral adrenalectomy, may also be induced in patients who have been receiving therapy with cortisone or other corticosteroids. The possibility of death following surgical intervention in such persons has been pointed out.* This is particularly apt to occur in cases where emergencies require surgery to be performed without benefit of prior work-up and preparation.

We wish to describe our experiences in the management of three patients with adrenocortical insufficiency, each with a different problem, who required surgical intervention. We have had six patients with hypoadrenalism at the Hospital for Special Surgery in the past two years who required surgery; hence, it is by no means a rare problem. Five of the six patients had cortisone-induced cases of hypoadrenalism. All were prepared for surgery but one, and in only one who required emergency surgery did death occur. The data on three of these patients are being presented in this paper to illustrate the methods whereby we managed the problems.

One patient had been receiving intensive hydrocortisone therapy for rheumatoid arthritis when he developed acute appendicitis. A second patient had suppressed adrenocortical function produced by cortisone therapy for pemphigus, and he required an elective femoral replacement arthroplasty of the hip. A third patient had known Addison's disease and needed spinal and sacroiliac fusions. Each of these patients presented different problems in the management of their adrenocortical deficiency. The successful results obtained in all but one case were due mainly to the extended metabolic work-up prior to, during, and after surgery. The scale of trauma in the surgery of these cases is very intense.

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* References 1, 2, 3, and 4.

REPORT OF CASES

CASE 1. — *Example of Hydrocortisone-Induced Adrenocortical Insufficiency Requiring Emergency Surgery*

A man 47 years of age entered the clinic for rheumatic diseases of the Hospital for Special Surgery in 1940 because of rheumatoid arthritis involving the neck, shoulders, wrists, and knees. Gold therapy was started but was discontinued because it produced severe dermatitis. On Aug. 14, 1949, he was given 25 mg. of corticotropin (ACTH) by intramuscular injection, which resulted in good relief of his pains with diminution of his stiffness. Therefore, he was started on corticotropin therapy of 50 mg. twice a day. In January, 1950, his treatment was changed to desoxycorticosterone acetate (DCA) in 5 mg. doses on alternate days, combined with ascorbic acid. In November, 1951, his treatment was changed to hydrocortisone with phenylbutazone. This was maintained thereafter on low dosage. Despite this, he gained weight and developed some facial edema at times.

On Nov. 7, 1954, the patient was brought to the hospital in acute distress due to appendicitis. Ap-

pendectomy with drainage of a retrocecal abscess was performed during cyclopropane anesthesia. Preoperatively he was given an infusion of 1000 cc. of 5% dextrose in water. During the operation, intravenous therapy was continued with 250 cc. saline and 500 cc. of blood because the patient's hemoglobin was 11.4 gm. per 100 cc. of blood. All other vital signs were within normal limits. During the operation his arterial blood pressure, pulse rate, and respiratory rate remained normal. But immediately postoperatively, as he was emerging from anesthesia, severe surgical shock developed, characterized by low arterial blood pressure, rapid thready pulse, and cold clammy skin. The intravenous administration of 100 mg. of hydrocortisone free alcohol in 1000 cc. of 5% dextrose in saline resulted in considerable improvement within a half hour. Nine days later, viscera broke through the wound. Closure was made with through-and-through nonabsorbable surgical (silk) sutures during cyclopropane anesthesia, at which time an intravenous infusion of 1000 cc. of 5% dextrose in saline containing 100 mg. of hydrocortisone was administered. Immediately postoperatively he again manifested severe surgical shock, and he was treated with good results by the intravenous administration of another 100 mg. of hydrocortisone. Four days later a fecal fistula developed. The patient died a week later, after an episode of pyrexia which was not affected by antibiotic therapy. Autopsy revealed massive septicemia, with abscesses scattered throughout the peritoneum, the peribronchial tissue, and the myocardium. The adrenals were atrophic. One adrenal gland weighed 3.2 gm., the other 2 gm., with marked thinning of the cortex.

This case illustrates that prolonged therapy with hydrocortisone can result in hypocorticalism and that when such a patient requires surgical intervention, even of a relatively minor nature, he may require supplemental hydrocortisone to treat a crisis of acute adrenocortical insufficiency. Hypocorticalism was demonstrated both anatomically and functionally: anatomically, by the atrophy of both adrenal glands, with thinning of the cortex, and, functionally, by the states of surgical shock which developed following each of two relatively minor surgical procedures. In each instance, this complication occurred as soon as anesthesia wore off. In the first instance blood tranfusion which was considered greater in quantity than the amount of blood lost during the appendectomy was ineffectual in preventing the postanesthetic shock. In both instances the hypotensive state was corrected by the intravenous administration of additional hydrocortisone.

This case illustrates two other important points. First, patients receiving corticosteroid therapy may develop susceptibility to certain infections poorly responsive to antibiotics. Second, the administration of general anesthesia to such patients undergoing surgery may block or delay the state of acute adrenal cortex insufficiency until the effects of anesthesia are dissipated.

This case was the only fatality in our series, and death occurred not from hypocorticalism but from the massive sepsis, which may have been enhanced by our treatment of his insufficiency.

CASE 2.—*Example of Elective Surgery in a Patient with Cortisone-Induced Hypocorticism*

A lawyer 43 years of age had been treated for pemphigus with cortisone for 5 years. His daily dose of cortisone had ranged from 200 to 1000 mg. Complications which ensued included cortisone-induced psychosis, which was treated by electroshock therapy, cortisone-induced osteoporosis, and bilateral avascular necrosis of the femoral heads together with avascular necrosis of the left humeral head. The patient developed so much pain and stiffness in his legs that he sought help and agreed to a prosthetic replacement of his left femoral head, which was performed on Jan. 13, 1954.

Preoperative laboratory findings disclosed that this patient had certain stigmata of hypoadrenalism. These included a failure to retain water, with high urinary output and arterial hypotension. When given 50 mg. of corticotropin in a 4-hour infusion, he did not retain salt nor did his 17-ketosteroid excretion rise. His total eosinophile count did not drop after this test. It was clear that this patient needed salt and adequate cortisone therapy, the dosage of which was to be determined by daily metabolic studies. He was given 2 liters of isotonic saline intravenously the first 24 postoperative hours and cortisone intramuscularly every 4 hours in doses of 50 to 100 mg. at a time, so that his daily dosage ranged between 400 and 600 mg. for 3 days. After the third day, results of the patient's blood chemistry studies were within normal limits and his urinary output and salt loss were normal. The first 2 days were characterized by wide swings in blood pressure and salt excretion. Twenty-four and 12 hours preoperatively he was given 100 mg. of cortisone intramuscularly.

On the day of operation the patient was given preanesthetic medication consisting of procainamide hydrochloride, 500 mg. orally, 75 minutes before anesthesia, and morphine sulphate, 10 mg., combined with scopolamine hydrobromide, 0.4 mg., injected hypodermically one hour before anesthesia. The intramuscular administration of cortisone was maintained. Anesthesia was induced by the intravenous injection of 400 mg. of hexobarbital sodium (Evipal Sodium) in a 2% aqueous concentration. This was followed by the administration of cyclopropane-oxygen anesthesia. During the operation, fluid therapy consisted of saline (1000 cc.), 6% dextran (500 cc.), blood (500 cc.), and 5% dextrose in water (500 cc.).

The patient was managed with saline and cortisone alone, and he was brought through the planned surgical procedure successfully. However, he required constant attention because he had nine bouts of hypotension in the first 72 hours. Salt excretion during this time was high, being 300 mEq. for the first 24 hours postoperatively.

We do not advocate this method for coping with the problem, but it is interesting to note that, despite the loss of a check rein on salt loss, patients requiring large-scale surgery can successfully survive.

CASE 3.—*Example of a Patient with Adrenal Insufficiency Due to Addison's Disease Requiring Elective Surgery* †

A man 37 years of age had Addison's disease for seven years. He had been managed fairly successfully for several years on a program of desoxycorticosterone acetate pellets of 150 mg. implanted every three months and cortisone in doses of 25 mg. daily orally. Owing to a back injury, he had a great deal of pain which interfered with his daily routine. Orthopedic consultation suggested that he might be helped by a lumbosacral fusion together with a sacroiliac fusion. Because of the severe degree of trauma involved in these operations and because of the patient's adrenocortical insufficiency due to Addison's disease, it was deemed dangerous to proceed with these operations. However, since this young man would become incapacitated without surgical intervention, it was decided, reluctantly, to perform the operations by doing the two different procedures at different times if necessary and by having a team versed in endocrinology and surgical physiology help in the management of this patient before, during, and after the operation.

† Dr. Ephraim Shorr, of the New York Hospital, provided advice in the management of this case.

It was planned to manage this patient with hydrocortisone intravenously throughout the surgical period and postoperatively as needed, supplementing this with desoxycorticosterone, saline, and cortisone as indicated. At 24 and 12 hours preoperatively he was given 100 mg. of cortisone intramuscularly.

The operation was accomplished on Oct. 21, 1954. Preanesthetic medication consisted of an opium preparation (Pantopon), 10 mg., and atropine sulphate, 0.4 mg., injected hypodermically one hour before induction of anesthesia. Anesthesia was obtained by the intravenous injection of 300 mg. of hexobarbital sodium in a 2% aqueous concentration followed by cyclopropane with oxygen. Endotracheal intubation was performed with a cuffed No. 36 Magill tube, and the patient was turned onto the prone position. Preanesthetic arterial blood pressure was 100 mm. Hg systolic and 64 mm. diastolic. The pulse rate was 72 per minute. These circulatory levels were maintained remarkably stable throughout the entire operation, which lasted more than 3 hours. The electrocardioscope which was observed during the procedure showed a regular sinus rhythm at all times. Fluid therapy consisted of 2000 cc. of blood to compensate for a similar amount of blood loss produced by the lumbosacral fusion followed by the sacroiliac fusion (both were done, since the patient's condition remained good). In addition, the patient received 100 mg. of hydrocortisone in 1000 cc. of 5% dextrose in saline, which was administered intravenously during the surgical procedure.

The postoperative course was satisfactory in that no Addisonian crisis developed at any time during the next 2 months. The urinary salt excretion during this time varied between 5 and 10 gm. a day, necessitating some replacement, and the arterial blood pressure was maintained within normal limits. To prevent negative salt balance, adequate amounts of desoxycorticosterone and saline were periodically administered. Minor complications, consisting of a urinary tract infection on the third postoperative day, a transfusion reaction characterized by mild angioneurotic edema, and a mild wound infection despite antibiotic therapy, occurred. In each instance increased cortisone and salt were given. Four months later, the patient was subjected to another surgical intervention for the removal of a Wilson plate which had been used in the spinal fusion as a form of fixation. The same program of management as used in the previous operation was employed, except that anesthesia was provided by means of local infiltration with 1% hexylcaine (Cyclaine) solution together with thiopental sodium by intravenous drip merely sufficient to cause drowsiness. No sequelae were noted other than the need for increased cortisone and added amounts of salt

and desoxycorticosterone immediately postoperatively. Water retention was never a problem.

This case is noteworthy because desoxycorticosterone provided a check rein on the tendency to develop salt loss and arterial hypotension. Desoxycorticosterone, it will be recalled, is an adrenocortical-like steroid that permits reabsorption of salt in the kidneys so that urinary salt loss is minimized. Though this patient had marked adrenocortical insufficiency, though the magnitude of his surgery was great, and though complications ensued postoperatively, this patient had a smooth postoperative course insofar as no Addisonian crisis ever developed.

ANESTHESIOLOGICAL CONSIDERATIONS

As to the effect of anesthesia on adrenocortical function during surgical trauma, previous studies have shown that uncomplicated general anesthesia modifies the usual response of the adrenal cortex to surgical stress.‡ By using the eosinophile count as an index of adrenocortical activity, it has been shown that the stress of surgical trauma produces a marked fall in the eosinophile count in the circulating blood.§ With use of this eosinopenic response with a fall of more than 50% of the eosinophiles as a criterion, it was observed that eosinopenia did not occur in 83% of the patients during uncomplicated general anesthesia for operations lasting more than 2 hours but that it did appear when the anesthesia wore off.[6] Similar studies during uncomplicated spinal anesthesia with surgery were less conclusive, in that 40% of the patients showed an eosinopenic response both during spinal anesthesia with surgery and after spinal anesthesia had worn off.[6] Although eosinophile counts in themselves provide only a rough estimate unless carefully done, they, along with urinary salt excretion, are useful aids in the day-to-day management of these patients.

Since acute adrenocortical insufficiency is accompanied by impaired homeostatic adjustments to stress, with inability to compensate for various circulatory disorders, it is important to avert stress-imposing reactions. Thus, high spinal anesthesia or deep general anesthesia, both of which may cause arterial hypotension, should be avoided. Sympathetic blockade produced by drugs such as pentamethonium, hexamethonium, or trimethaphan camphorsulfonate (*d*-3,4[1′,3′-dibenzyl-2′-ketoimidozolido]-1,2-trimethylene thiophanium *d*-camphor sufonate) (Arfonad) should also be avoided, since pharmacological sympathetic blockade so produced may result in marked arterial hypotension from which recovery might be difficult. Respiratory depression from any cause should be prevented at all times. An excitement stage during induction of anesthesia should be averted by proper preanesthetic medication and by use of a small dose of an intravenous barbiturate. The management of postoperative pain should aim at securing pain relief without causing respiratory or circulatory depression.

COMMENT

The endocrinological and metabolic management of patients with hypocorticalism who require elective surgical therapy is important. It is suggested that such patients be made research projects for a biochemical team wherever feasible, in order to determine their metabolic status.

The preoperative estimation of hypocorticalism depends upon various factors. In the case of known Addison's disease, the diagnosis is obvious. Induced hypocorticalism resulting from prolonged therapy with cortisone or other corticosteroids should be suspected in any patient receiving such therapy prior to surgical intervention. Patients who have been treated with cortisone for only one or two weeks may, rarely, have suppressed adrenocortical function. In such cases corticosteroid therapy should be continued if surgery is required. If the patient has been receiving his treatment by oral administration, therapy should be maintained parenterally when the oral route is discontinued on the day of operation. There is an analogy here to diabetic patients requiring insulin therapy: in both instances endocrine therapy must be maintained, increased as necessary, but never interrupted. Although we have not seen prednisone (Meticorten)-

‡ References 5 and 6.

§ References 7, 8, and 9.

induced insufficiency, we presume that it, too, will be shown to occur.

When time permits, certain laboratory determinations are useful in planning individual management before, during and after surgery. Biochemical tests that are important include the eosinophile counts and electrolyte excretion in response to intravenous corticotropin; estimation of the 17-ketosteroids, the 17-hydroxycorticoids, and the acid steroid fraction[11] in the urine; measurement of daily urinary output; estimation of daily urinary salt excretion; determination of blood levels of sodium, potassium, chloride, and CO_2-combining power, and water load tests.

The following suggestions are advocated in the management of patients with hypocorticalism who require surgical intervention and anesthesia, although each case requires individualized treatment.

1. Increase the amount of corticosteroid preoperatively if the patient has been receiving such therapy. Never cease or decrease it unless it is possible to postpone surgery until a normal adrenal response has been reestablished.

2. Increase the salt intake during and after surgery. If salt loss is occurring, 6 to 9 gm. of sodium chloride may be necessary for the total daily replacement.

3. Estimate blood loss and fluid loss accurately and administer these amounts to the patient. Ascertain whether the patient is sweating and provide for appropriate salt replacement.

4. Be prepared to treat arterial hypotension that is not due to blood loss by the intravenous administration of hydrocortisone. This should be given by placing 100 mg. in a liter of saline and administering this quantity in from one to four hours.

5. Watch for signs of fluid retention by palpating the patient's bony prominences.

6. If increased stress, such as a postoperative infection, occurs, increase the amount of salt intake and of cortisone if necessary. However, decrease the cortisone thereafter as rapidly as possible. It may be advisable to change to desoxycorticosterone to diminish salt loss in excessive quantity rather than rely on high cortisone administration.

7. As soon as a salt balance can be obtained and maintained by oral intake, the dosage of corticosteroid should be diminished gradually but as rapidly as possible.

8. To maintain good nutrition, large amounts of protein are indicated. Sometimes it may be advisable to enhance this effect by the administration of testosterone.

9. These patients should be watched carefully day and night from the time of surgery until a proper metabolic and electrolyte balance is obtained. Asthenia, lassitude, weakness, and arterial hypotension indicate impending adrenocortical crisis. A low CO_2-combining power, excessive urinary salt loss, and low serum chloride and sodium also should alert one to the need for treatment. Hypokalemia must also be guarded against when using these steroids even as replacement.

10. In case of salt retention (as evidenced by edema) the amount of salt intake should be diminished. Desoxycorticosterone should be discontinued if it is being given then, but hydrocortisone or cortisone should be made available. If necessary, it may be wise to provide some potassium if too much sodium retention is present.

11. The urinary output should be measured and charted. Daily urinary output of more than 2000 cc. postoperatively the first 3 days should be suspected of containing an excess of salt loss, unless as a result of high fluid intake. Water intoxication and salt-losing nephritis should be ruled out.

12. If the patient has some cardiac disease with diminished cardiac reserve, other therapeutic aids should be given as indicated and the salt load must be watched carefully.

SUMMARY AND CONCLUSIONS

The management of three patients with adrenocortical insufficiency, each with a different set of conditions and each requiring surgery, is described. One patient had hypocorticalism induced by prolonged hydrocortisone therapy for rheumatoid arthritis; he survived two emergency operations but finally succumbed to septicemia. A second patient had cortisone-induced hypocorticalism and required a rather large-scale elective operation. The third patient was a known Addisonian who required an elective spinal fusion and sacroiliac fusion. All three patients were protected from the development of an adrenal crisis, though each of the patients was managed in a different manner. All required cortisone or hydrocortisone postoperatively in increased amounts. The management will vary, however, from patient to patient, depending upon many factors.

Some anesthesiological considerations on this problem are given. In the main these include avoidance of stress-imposing reactions, such as arterial hypotension and respiratory depression.

Patients who need surgical intervention and who have depressed adrenocortical function as a result of therapy with some corticosteroid may be managed safely through surgery of rather severe degree. If the proposed surgical procedure is of an elective nature, the optimum method of management would be to postpone the time of surgery until corticosteroid therapy has been discontinued and a sufficient length of time has elapsed to allow demonstration of normal adrenal reserve. If corticosteroid therapy must be continued, then it should not be discontinued during the time of surgical management; rather, corticosteroid therapy should be increased preoperatively, whether the surgical problem is an emergency or not. In the case of an elective procedure under such circumstances, the management is similar to that of the patient with known Addison's disease. The preoperative period should be utilized to evaluate the patient's metabolic and electrolyte requirements. Increased cortisone 24 hours before surgery is advised. During surgery, hydrocortisone should be given intravenously and sufficient salt intake should be given to the patient at all times. Postoperatively, corticosteroid therapy should be maintained as required by the patient in the immediate convalescent period, but it should be reduced gradually as rapidly as possible to prevent the possibility of sepsis and infection. Desoxycorticosterone is a very valuable salt-saving adjunct and should be used if necessary.

It is important to bear in mind that adrenocortical insufficiency may persist for many weeks after prolonged corticosteroid therapy has been discontinued. The adrenocortical response of patients who require surgical intervention should be investigated carefully in order to avert acute adrenocortical insufficiency.

REFERENCES

1. Fraser, C. G.; Preuss, F. S., and Bigford, W. D.: Adrenal Atrophy and Irreversible Shock Associated with Cortisone Therapy, J. A. M. A. **149**:1542-1543, 1952.

2. Lundy, J. S.: Cortisone Problems Involving Anesthesia, Anesthesiology **14**:376-381, 1953.

3. Salassa, R. M., and others: Clinical Aspects of Suppression of Adrenal Cortical Function After Use of Cortisone, Proc. Staff Meet., Mayo Clin. **28**:662-668, 1953.

4. Lewis, L., and others: Fatal Adrenal Cortical Insufficiency Precipitated by Surgery During Prolonged Cortisone Treatment, Ann. Int. Med. **39**: 116-126, 1953.

5. Traina, V., and Burstein, C. L.: Effect of Anesthesia on the Eosinopenic Response to Surgical Trauma: Preliminary Report, Am. J. Surg. **84**:13-15, 1952.

6. Traina, V.; Burstein, C. L.; Ciliberti, B. J., and Rovenstine, E. A.: Pituitary-Adrenal Response to Surgical Trauma and Anesthesia: I. The Eosinopenic Response, Anesthesiology **14**:449-455, 1953.

7. Almy, T. P., and Laragh, J. H.: Reduction in Circulating Eosinophils Following Epinephrine, Insulin and Surgical Operation, Am. J. Med. **6**: 507, 1949.

8. Roche, M.; Hills, A. G., and Thorn, G. W.: The Levels of Circulating Eosinophils as an Indicator of Adrenal Cortical Adequacy Following Major Surgery, J. Clin. Endocrinol. **2**: 662, 1949.

9. Hayes, M. A.: Shock and the Adrenocortex, Surgery **35**:174-190, 1954.

10. Nicholas, J. A., and Wilson, P. D.: Adrenocortical Function in Operative Procedures Upon Bones and Joints, J. Bone & Joint Surg. **35 A**: 559-572, 1953.

11. Nicholas, J. A.; Wilson, P. D., and Umberger, C. J.: A Comparison of Urinary Neutral 17-Ketosteroid Excretion with Other Fractions in Operations upon the Bones and Joints, Surg., Gynec. & Obst. **100**:387-390, 1955.

Upper Dorsal Sympathectomy Without Horner's Syndrome

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The sympathetic pathways to the muscles of the iris concerned with pupillary action have been described by many investigators both in animals and in man.* It has been generally agreed that the cell bodies of the preganglionic neurons are in the eighth cervical and the first and second thoracic (dorsal) levels of the spinal cord. The greatest number apparently are found at the first thoracic level. These preganglionic neurons leave the spinal cord, as recorded in the literature surveyed, mainly by way of the first and second thoracic ventral roots and enter the sympathetic chain at these levels via the rami communicantes. They pass cephalad through the inferior cervical or the stellate ganglion (a fusion of the first thoracic with the inferior cervical ganglion) to synapse with the postganglionic neurons located in the superior cervical ganglion. These latter fibers then pass via the carotid vessels or nasociliary nerves to the ciliary muscles, which control pupillary action. Stimulation of these fibers produces a dilatation of the pupil; paralysis of these pathways results in a constricted (miotic) pupil.†

Several authorities have indicated that some of the sympathetic pathways to the eye pass through separate paravertebral ganglia closely associated with the ventral roots of the eighth cervical and first and/or second thoracic nerves and that these preganglionic neurons do not enter the thoracic sympathetic chain but do enter it at the upper level of the stellate ganglion. This latter pathway pattern is not commonly found in man.‡

Interference with these pathways outside the central nervous system by disease, tumors, surgical division, or trauma usually results in a Horner syndrome. This syndrome is characterized mainly by a constricted pupil (miosis), lagophthalmos (narrowing of the palpebral fissure), and enophthalmos. It has been reported by many that interruption of the ventral roots of the first and second thoracic nerves or removal of the lower portion of the stellate ganglion or the first and second thoracic ganglia resulted in the production of Horner's syndrome. It likewise has been shown that if the lower portion of the stellate ganglion is not destroyed, but the upper part is, Horner's syndrome develops.§

From the data presented above, it appears that definite pathway patterns in man have been reported in the literature and in anatomy books to indicate that Horner's syndrome will occur after the destruction or interruption of these pathways. The purpose of this presentation, as a preliminary report, is to show that the sympathetic pathways as described above to the ciliary muscles do not conform to those previously reported in man.

Since April, 1953, a total of 14 consecutive upper dorsal sympathectomies have been performed upon 10 male patients, ranging in age from 35 to 62 years. In four cases, a bilateral procedure was accomplished, whereas in the remaining six cases it was performed unilaterally.

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From the Department of Surgery, Veterans Administration Hospital.

* References 1, 3 to 6, 8, 11 to 14, 18, 19, and 21.

† References 3 to 6, 8, 10 to 14, 19, and 21.

‡ References 2 and 12.

§ References 3, 5 to 8, 10, 12 to 14, 17, and 19 to 21.

INDICATIONS FOR SYMPATHECTOMY

The sympathetic denervation was performed in two cases for the treatment of intractable angina pectoris associated with coronary occlusion, in one for angina pectoris secondary to coronary atherosclerosis and peripheral arteriosclerosis (more advanced in the upper extremities), and in the remaining cases for Büerger's disease (thromboangiitis obliterans) or peripheral vascular diseases.

OPERATION

The surgical approach was made through an anterior, transpleural, transthoracic wound. The patient was placed in a supine position with about a 15-degree elevation of the chest on the operative side. The upper extremity was placed in abduction and external rotation in order to expose the upper anterior aspect of the thorax. Endotracheal anesthesia, with the use of nitrous oxide-ether and curare supplemented with other agents, was administered. An anterior skin incision was made over the course of the fourth rib from the parasternal line to the midaxillary line. The fourth rib was resected aperiosteally in the first four operations from the costal cartilage anteriorly to the midaxillary line. The costal cartilage of the third rib anteriorly was divided. The pleural cavity was entered through the bed of the fourth rib. However, in the remaining cases an intercostal incision through the third interspace was performed. The upper lobe of the lung was depressed downward and medialward.

The parietal pleura overlying the angle of the ribs was divided in a vertical direction from the upper border of the first rib to below the fifth rib. The thoracic (dorsal) sympathetic chain was then dissected free from the surrounding structures. It was divided below the fifth thoracic ganglion; all of the rami, medial and lateral communications, and branches were divided. The dissection was carried upward to the lower border of the first rib at which point the rami and medial communications were divided. The sympathetic chain was then sectioned above the first thoracic ganglion in

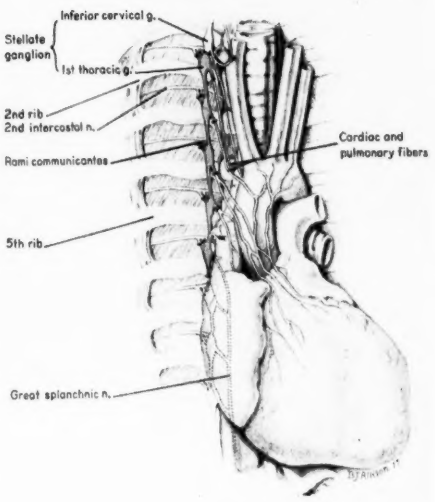


Fig. 1.—The normal relationship of the right upper thoracic sympathetic chain and ganglia as seen through an anterior intrathoracic wound. The points of sectioning of the chain, ganglia, rami, and medial fibers, and the portion resected (first through the fifth thoracic) are outlined in this drawing.

those cases where it was not completely fused with the inferior cervical ganglion. In those cases where it was partially or completely fused to form a typical stellate ganglion, the division was made across this large ganglion immediately above the site of the rami for the first intercostal nerve. In other words, the lower one third of the stellate ganglion was resected. Therefore, the sympathetic chain from the first down through the fifth thoracic ganglion was resected (Figs. 1 and 2).

The exposure obtained was excellent, permitting complete and easy visualization and accessibility to this portion of the sympathetic chain so that the operator could be sure of the scope and extent of the denervation. Also, he could be sure of dividing all of the communications, branches, and rami leading to and from the chain at these levels. This is one of the important considerations of this type of approach and exposure. There is very little chance of performing an incomplete interruption of the upper thoracic rami

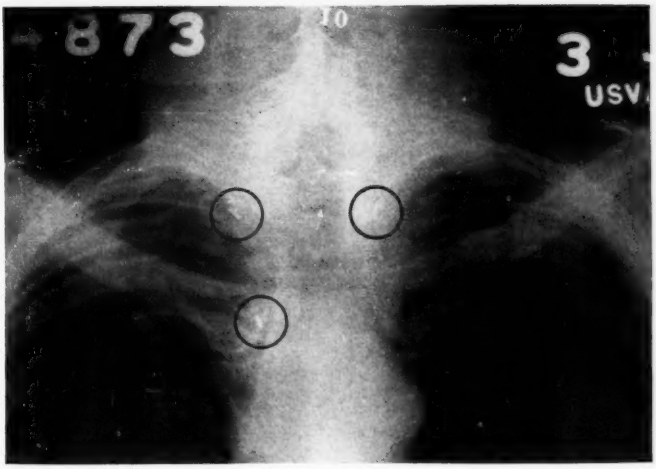


Fig. 2.—The upper silver clips shown on the right side of this x-ray of the chest reveal the site of the division of the thoracic sympathetic chain through the lower part of the stellate ganglion. The left lateral clip was placed on the divided ends of the rami communicantes of the first intercostal nerve. The lower clip on the right side was placed on the upper end of the divided sympathetic chain below the fifth sympathetic ganglion.

Fig. 3*A* and *B*.—Sweating patterns (Minor's starch-iodine method) showing loss of sweating (light areas) of the left half of the face, neck, shoulder, upper extremity, and anterior and posterior portions of the chest down to the fourth or fifth intercostal levels. This patient was treated for angina pectoris and coronary occlusion. The light areas on all photographs of sweating patterns represent areas of absence of sweating.

if the surgeon is careful in identifying the posterior pleural surface of the first rib.

The chest wound was closed in layers with interrupted black nonabsorbable (silk) sutures. The lung was reexpanded under direct vision, and an intercostal chest tube under-

Fig. 4*A* and *B*.—Bilateral dorsal sympathectomy; on right, first through the fifth, and on the left, first through sixth levels. Complete loss of sweating, bilaterally, face, neck, shoulders, upper extremities, and anterior and posterior upper portions of chest. The bilateral incisions are apparent above the nipples. This patient was treated for peripheral vascular disease of the upper extremities and angina pectoris secondary to atherosclerosis.

water drainage was provided. The tube was placed usually in the anterior axillary line two to three interspaces below the incision. The intercostal tube was removed in 48 hours.

RESULTS

Horner's syndrome did not occur after 13 dorsal sympathectomies. All of the patients lost sweating of the head and neck, shoulder, upper extremity, and anterior and posterior portions of the chest down to the fifth thoracic levels on the side operated on (Figs. 3*A* and *B*, 4*A* and *B*, 5*A* and *B*, and 6*A* and *B*).

In the fourth consecutive patient, treated for peripheral arteriosclerosis and coronary sclerosis, the routine technique was employed on the right side without the development of Horner's syndrome. When the left-sided procedure was accomplished, we recorded the surgical technique by a colored movie, and in order to demonstrate the stellate ganglion more fully it became necessary to perform a higher dissection of this ganglion than usual, both on its medial and on its lateral aspects. However, the sectioning of the ganglion was, as formerly, just above the rami to the first thoracic nerve. After this procedure the patient developed a Horner syndrome on the left side. This is shown in Figure 6*C*, which was taken Dec. 16, 1954, several months postoperatively. We assume from these studies that in this particular operation the dissection of the stellate ganglion for a short distance above the ramus to first thoracic nerve must have interrupted the pupillociliary pathways which enter or leave the stellate ganglion in this area.

In one case, a patient with severe angina pectoris and residuals of two coronary occlusions, only a left-side sympathectomy from the first to the fifth was performed.

Fig. 5*A*.—Left, unilateral, dorsal sympathectomy, first through

Fig. 5*A*.—Left, unilateral, dorsal sympathectomy, first through the sixth, for treatment of severe intractable angina pectoris secondary to two coronary occlusions. Typical loss of sweating on left side, including face, neck, shoulder, upper extremity, and anterior and posterior aspect of chest to the sixth dermatome level. However, there is loss of sweating of right lower half of face, right shoulder anteriorly, and most of the right upper extremity anteriorly. This patient exhibits cross innervation of the sympathetic supply of the left side supplying part of the areas on the right anterior aspects of the body. This patient showed no evidence of preoperative or postoperative neuropathy. These sweating patterns have not changed in 15 months. These were taken Dec. 23, 1954, 15 months postoperatively. Two previous tests were made about the eighth postoperative day and then three months later.

Fig. 5*B*.—Typical unilateral loss of sweating posteriorly, on left side only.

Figures 5*A* and 5*B* are reproduced by courtesy of Palumbo, L. T.: Management of Disorders of the Autonomic Nervous System, Chicago, Year Book Publishers, Inc., 1955, p. 109.

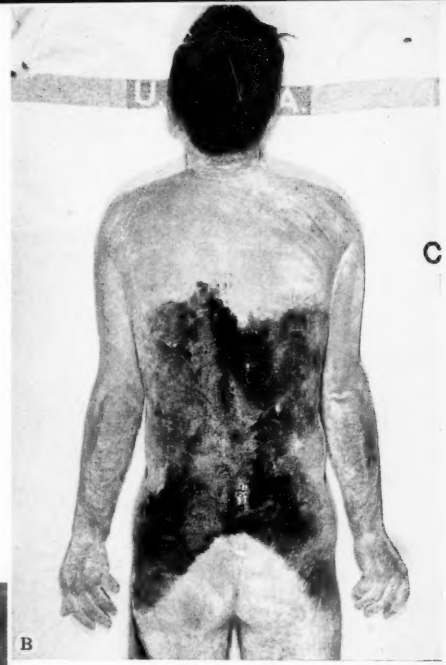
Fig. 5*C*.—This photograph, taken 15 months postoperatively, Dec. 22, 1954, was taken on the same day that the patient (Figs. 5*A* & *B*) had his third postoperative sweating test. The pupils are equal in both shape and size. There is no evidence of drooping of the left upper eyelid or narrowing of the palpebral fissure. This photograph was taken at normal room illumination. Exposure was by high-speed gaseous discharge flash tubes with a duration of approximately 1/4000 second.

A

Fig. 6A and B.—Typical loss of sweating anteriorly and posteriorly as noted in light areas on face, neck, chest, back, and upper extremities after the anterior transthoracic approach to the upper dorsal sympathetics was used, with removal from the first through the fifth thoracic ganglia. The incisions are visible just beneath both nipples.

Fig. 6C.—In this case the typical technique, as used in all of the preceding cases in this series, was performed on the right side, with no Horner's syndrome resulting; however, when the left side was operated on a greater mobilization of the stellate ganglion was purposely accomplished in order to obtain better visualization of this area during the filming of this procedure by colored motion pictures. This was followed by Horner's syndrome on the left side, as seen in this photograph, taken two months postoperatively. The left pupil is smaller than the right. The left upper eyelid droops slightly, causing a narrowing of the palpebral fissure. This photograph was taken under normal room illumination, exposure by high-speed gaseous discharge flash tubes with a duration of approximately 1/4000 second. This case is a good one for comparison to exemplify the fact that when our basic technique is strictly adhered to Horner's syndrome does not develop; however, if mobilization of the stellate ganglion is too extensive, the pathways above the first dorsal rami may be inadvertently destroyed, resulting in Horner's syndrome.

C



B

His sweating patterns, recorded about the 10th postoperative day, after 3 months, and again 15 months postoperatively, revealed a complete denervation on the left side, as would be expected. However, on the untreated side, the right side, there was a loss of sweating of the face from the eyebrow to below the lower jaw, the shoulder, upper portion of the chest anteriorly, and portions of the upper extremity anteriorly (Figs. 5*A* and *B*). This apparently represents cross innervation, with the sympathetics from the left side supplying these areas as shown on the right. This patient revealed no evidence preoperatively or postoperatively of neuropathies which might cause disturbances in his sweating mechanism of any part of his body.

The sweating patterns of the case above were recorded on Dec. 22, 1954. The pupils shown in Figure 5*C* are of the same case taken on the same day. Only a left sympathectomy was performed. The two pupils are equal in size and shape, and there is no evidence of ptosis of the left upper eyelid or of enophthalmos.

The therapeutic results in all cases were excellent for relief of pain and increase of peripheral circulation to the extremities denervated. A discussion of the value of this procedure for a variety of conditions is not the primary purpose of this report. This will be reported at length at a later date. It was the primary purpose to show that a Horner syndrome did not occur when these pathways were interrupted.

COMMENT

It must be assumed from these 10 consecutive cases that the sympathetic pathways innervating the ciliary muscles of the eye concerned with pupillary dilatation did not traverse the upper dorsal sympathetic chain. The division of all the communicating rami of the first through the fifth thoracic levels of the sympathetic chain with removal of the sympathetic chain from the lower portion of the stellate ganglion down through the fifth thoracic ganglion did not produce a Horner syndrome, as it should have done according to former reports recorded in anatomy texts and in the surgical literature.

It is assumed that in these cases the ciliary pathways from the first and/or second thoracic levels of the cord leave the ventral roots via separate pathways to reach the upper portion of the stellate ganglion and that these preganglionic neurons do not pass via the communicating rami to the sympathetic chain in the upper dorsal region. It appears, as has been shown by others,‖ that the sudomotor (sweating) fibers to the head, neck, and upper extremity are completely separate from the motor ciliary pathways, since the interruption of the sympathetics as outlined above resulted in the loss of sweating in the areas demonstrated in the photographs of the patients presented.

All these patients were carefully examined and observed prior to surgery to rule out any diseases or conditions of the nervous system which might cause a variation or change in their sweating mechanism; no neuropathies were present. Every case was examined on various occasions preoperatively and postoperatively by several members of the house and full-time staffs, as well as by me, for pupillary changes. In none, except the one side of one case, did pupillary changes occur. The reason for this has been explained elsewhere in this article.

SUMMARY AND CONCLUSIONS

Resection of the upper dorsal sympathetic chain, including the removal of the first thoracic, or lower, portion of the stellate ganglion to and below the fourth or fifth dorsal ganglion, will not necessarily result in Horner's syndrome but will result in loss of sweating of the head, neck, shoulder, upper extremity, and the upper anterior and posterior aspects of the chest. It is assumed that the ciliary sympathetic pathways concerned with pupillary dilatation do not, at least in the 10 (13 sympathectomies) consecutive cases reported, pass via the communicating rami to the upper thoracic sympathetic chain but apparently reach the

‖ References 2, 3, 6, 9, 11, and 15.

upper portion of the stellate ganglion via separate pathways after leaving the spinal cord at these levels.

A new and apparently a more logical approach to this portion of the sympathetic chain is presented. It appears from this preliminary study that these patients, including the group with coronary heart disease and angina, will tolerate this position on the operating table and an intrathoracic procedure much better than the posterior chest, anterior cervical, or other approaches formerly described for an upper dorsal sympathectomy or stellate ganglionectomy.

Dr. H. Samberg, Chief, Section of Physical Medicine and Rehabilitation, helped in the interpretation of the sweating patterns.

ADDENDUM

Since the preparation of this article, 13 additional operations have been performed, making a total of 27 procedures. The ages ranged from 25 to 59 years, with an average age of 38 years. A variety of conditions and diseases involving the upper extremities and several cases of coronary heart disease with or without angina pectoris are included in this latter series. In six cases, the procedure was performed on the right side and in the remaining seven on the left. Of this number, five patients had a bilateral sympathectomy. In only one instance a permanent Horner syndrome occurred. This occurred on the right side of a patient who had a bilateral procedure. This patient was treated for scleroderma with an associated Raynaud phenomenon. The development of a typical Horner syndrome in this patient was apparently due to technical difficulties encountered as a result of extensive pulmonary adhesions due to a chronic adhesive pleuritis. This required extensive dissection, which, no doubt, caused destruction of the pupillociliary pathways in the upper segments of the stellate ganglion.

Three other patients developed a temporary miosis of slight degree. All these mioses occurred on the right side. The inequality of the pupils persisted for 13, 14, and 19 days, respectively, after which time the pupils returned to normal size and function and have been normal since.

Therefore, to date, only 7.4%, or 2 cases, developed a permanent Horner syndrome, both of which are explained on a technical basis and most likely are not due to the direct division of the first rami communicantes and the resection of the first dorsal (lower third of the stellate ganglion) sympathetic ganglion.

It is interesting to note that of the four cases which developed a temporary miosis, all occurred on the right side. This finding requires further observation before any specific significance can be attached to it, particularly from the standpoint of differences in technique or variations in the pathways on this side.

These additional cases fortify our results and aid in confirmation of our previous statements that the pupillociliary pathways in man apparently do not pass via the upper dorsal rami communicantes to the lower portion of the stellate ganglion but leave the ventral roots via a separate pathway to reach the upper part of the stellate ganglion.

Dr. S. Shapiro, Senior Surgical Resident, supplied the data which are included in the Addendum.

REFERENCES

1. Barnes, R.: The Role of Sympathectomy in the Treatment of Causalgia, J. Bone & Joint Surg. **35**:172, 1953.

2. Ray, B. S., and Console, A. D.: Residual Sympathetic Pathways After Paravertebral Sympathectomy, J. Neurosurg. **5**:23, 1948.

3. Ray, B. S.: Sympathectomy of the Upper Extremity, J. Neurosurg. **10**:624, 1953.

4. Craig, J. D., and Fuller, R. C.: Cervical Sympathetic Paralysis, Brit. M. J. **1**:1182, 1948.

5. Evans, J. A.; Poppen, J. L., and Tobias, J. B.: Relief of Angina Pectoris by Sympathectomy: Report of Results in 10 Patients Subjected to High Thoracolumbar Sympathectomy Including the Anginal Pathway, J. A. M. A. **144**:1432, 1950.

6. Grimson, K. S.: The Total Thoracic and Partial to Total Lumbar Sympathectomy and Celiac Ganglionectomy in the Treatment of Hypertension, Ann. Surg. **114**:753, 1941.

7. Guttmann, L.: The Distribution of Disturbances of Sweat Secretion After Extirpation of Certain Sympathetic Cervical Ganglia in Man, J. Anat. **74**:537, 1940.

8. Hyndman, O. R., and Wolkin, J.: Sweat Mechanism in Man, Arch. Neurol. & Psychiat. **45**:446, 1941.

9. Hyndman, O. R.; Wolkin, J., and Van Allen, M. W.: Cell Stations in the Upper Sympathetic Chain, J. Neurosurg. **5**:521, 1948.

10. Jaffe, N. S.: Localization of Lesions Causing Horner's Syndrome, Arch. Ophth. **44**:710, 1950.

11. Kuntz, A., and Dillon, J. B.: Preganglionic Components of the First Thoracic Nerve, Arch. Surg. **44**:772, 1942.

12. Kuntz, A.: The Neuroanatomic Basis of Surgery of the Autonomic Nervous System, Ed. 1, Springfield, Ill., Charles C Thomas, Publisher, 1949, p. 20.

13. Kuntz, A.: The Autonomic Nervous System, Ed. 4, Philadelphia, Lea & Febiger, 1953, p. 322.

14. Lindgren, I., and Olivecrona, H.: Surgical Treatment of Angina Pectoris, J. Neurosurg. **4**:19, 1947.

15. Palumbo, L. T.; Samberg, H.; Norris, L. D., and Kettenbach, E. L.: Sweating Patterns Following Dorsal and Lumbar Sympathectomy, Am. J. Surg. **80**:24, 1950.

16. Richter, C. P.: Cutaneous Areas Denervated by Upper Thoracic and Stellate Ganglionectomies Determined by the Electrical Skin Resistance Method, J. Neurosurg. **4**:221, 1947.

17. Saccomanno, G.; Utterback, R. A., and Klemme, R. M.: Anatomic Data Regarding the Surgical Treatment of Angina Pectoris, Ann. Surg. **125**:49, 1947.

18. Stine, G. H., and Draper, P.: Horner's Syndrome, Rocky Mountain M. J. **42**:504, 1945.

19. Welch, E. J.: Horner's Syndrome Complicating Surgery for Pulmonary Tuberculosis, A Review of 5 Cases, Am. Rev. Tuberc. **67**:94, 1953.

20. White, J. C., and Bland, E. F.: The Surgical Relief of Severe Angina Pectoris, Medicine **27**:1, 1948.

21. White, J. C.; Smithwick, R. H., and Simeone, F. A.: The Autonomic Nervous System, Ed. 3, New York, The Macmillan Company, 1952, p. 40.

Notice

A. M. A. Annual Meeting, Chicago, June 11-15, 1956.—The 105th Annual Meeting of the American Medical Association will be held in Chicago, June 11-15, 1956, with a full program of lectures, television, motion pictures, and scientific exhibits.

The lecture program for each Section is prepared by the Section Secretary, and prospective participants should communicate as soon as possible with the Secretary of the Section before which they hope to read a paper. Application blanks for space in the Scientific Exhibit are now available and may be obtained from the Section Representative to the Scientific Exhibit.

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Additional information may be obtained from the Secretary, Council on Scientific Assembly, American Medical Association, 535 N. Dearborn St., Chicago 10.

Pilonidal Sinus

Analysis of Two Hundred Six Operations Performed According to Varying Techniques

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and
PHILIP COOPER, M.D., Providence, R. I.

Although much as been written on the surgical treatment of pilonidal sinus, the subject remains unsettled. The literature abounds with a variety of statistics and opinions. Surgeons seem to fall into two groups: those who favor primary suture * and those who favor some type of open operation.† The former believe that recurrences should be no greater with primary closure than with the open operation. They add that, although the patient may require a longer period of hospitalization postoperatively, he does not require after-care following discharge from the hospital. Furthermore, the patient does not have the prolonged discomfort that accompanies an open wound. The latter believe, in general, that recurrence rates are lower, complications fewer, and hospitalization shorter than with the closed technique. They tend to minimize the inconvenience of an open wound.

After reviewing the statistics it becomes obvious that differences of opinion transcend philosophical considerations. For instance, following primary suture Gage [15] had no recurrence, while Rogers and Hall [16] reported 38% unsatisfactory results. Following open operation Zieman [17] had no recurrence; Larsen [11] reported 17%. Palumbo,[5] reviewing the literature, found 12.7% recurrence after open packing and 21.9% recurrence after primary closure. However, there were vast differences in the results of the various contributing authors.

The basis for these differences in statistics is difficult to determine. Suture material, skin preparation, antibiotics, avoidance of trauma, and proper choice of cases have all been stressed as important. Various techniques have been suggested: unroofing,‡ excision and suture of skin to fascia,[1] open packing,§ employment of gluteal fascial flaps,|| use of sliding flaps of skin and subcutaneous tissue,¶ and simple excision and closure.# However, the results vary in the hands of different surgeons.

In an attempt to discover some of the important factors which determine such variables, an analysis is made of 295 definitive operations for pilonidal sinus performed at the Veterans Administration Hospital, Providence, R. I., between June, 1949, and January, 1953. All patients were invited to return for careful follow-up examination. Two hundred patients, six of whom had undergone a second operation, reported between Oct. 8, 1953, and March 4, 1954. Thus, follow-up data are available for 206 operations, which are analyzed in detail below.

In general, preoperative and postoperative care for all cases was fairly well standardized. Patients with acute infection were treated by incision and drainage, sitz baths, and antibiotics as indicated. Definitive operation was

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* References 7 to 14.

† References 1 to 6.

‡ References 3 and 6.

§ References 2, 4, and 5.

|| References 7, 9, and 10.

¶ References 13 and 18.

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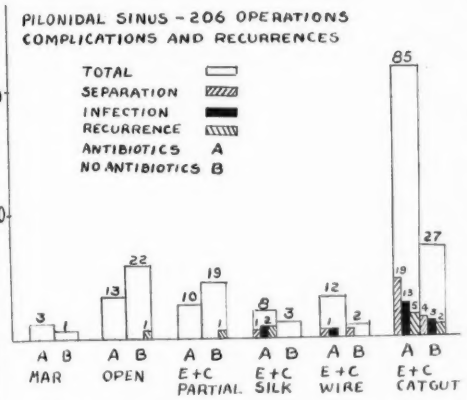

Fig. 1.—Complications and recurrences with and without antibiotics according to type of procedure. *Mar:* marsupialization. *Open:* excision and open packing. *E+C Partial:* partial excision and closure. *E+C Silk:* excision and closure with buried silk. *E+C Wire:* excision and closure with buried stainless steel wire. *E+C Catgut:* excision and closure with buried absorbable (gut) sutures.

performed only when all evidence of acute inflammation had subsided. The skin of the sacral region was carefully cleansed preoperatively. The type of operation performed was decided by the surgeon at the time of surgery. In both open and closed procedures block dissection was usually employed. Flaps of various types were rarely created. Closure was almost invariably effected by burying absorbable (gut) sutures, rarely silk or wire, to obliterate dead space; the skin was carefully approximated with nonabsorbable (silk) mattress sutures. After open types of operation the patient was ambulated usually on the first postoperative day. After the first few days daily dressings were performed and every effort was made to allow granulation to proceed from the depths of the wound. After primary suture the patient was confined to bed. He was then instructed not to lie on his back or flex his thighs for about 10 days to 2 weeks. About four days postoperatively, if there had been no previous evidence of infection, the first dressing was performed. Thereafter in uncomplicated cases the patient was allowed to ambulate. Infected wounds were opened wide and thereafter treated as open wounds. Wounds which had partially separated were merely packed lightly with gauze and allowed to granulate.

The use of antibiotics was left to the discretion of the surgeon. Figure 1 summarizes the results with and without antibiotics. It will be noted that in the 105 closed operations covered by antibiotics there were 16 (15.2%) infections, 21 (20.0%) separations, and 7 (6.7%) recurrence. Thirty-two closed operations performed without antibiotic coverage were followed by three (9.4%) infections, five (15.6%) separations, and two (6.3%) recurrences. These figures would not seem to indicate that antibiotics played an effective role in the reduction of complications.

Figure 1 also summarizes the results following the various types of operation performed. It will be noted that there were no infections in the 68 open operations. There were two (2.9%) recurrences for the whole group. In the 137 closed operations there were 26 (18.8%) separations, 19 (13.9%) infections, and 9 (6.6%) recurrences. It would appear, therefore, that complications are more frequent in the closed group.

Since this series is relatively small, it does not seem desirable to attempt to evaluate statistically the various types of closed and open procedures employed.

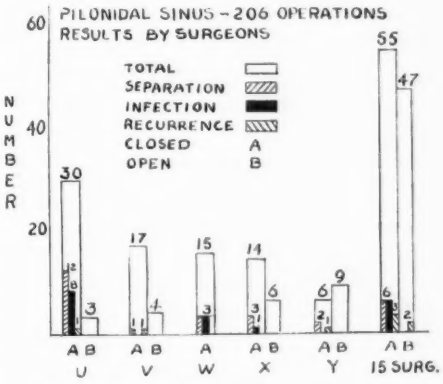

Fig. 2.—Complications and recurrences in 206 cases of pilonidal operations according to surgeons U, V, W, X, and Y. The results of the remaining 15 surgeons are summarized in the last column.

Since 20 surgeons who performed the operations were responsible for the type of procedure employed, it is of interest to examine their results. Reference to Figure 2 reveals a difference not only in their choice of operation but also in their results. For instance, surgeon U closed 90.9% of the wounds, with 70% complications; surgeon V, 81% of the wounds, with 11.8% complications, and surgeon W, all the wounds, with 60% complications. Since there is every evidence that each surgeon's series was comparable to the others', the results seem to depend a great deal on the surgeon's choice of operation and his ability to execute the surgery properly.

The average length of hospitalization following closed operations was 15.3 days, compared with 21.0 days following open operations. However, this tendency to hospitalize for prolonged periods patients with open wounds is not universally accepted among surgeons, many of whom prefer to treat such cases on an ambulatory office status. In view of these considerations it is not believed that length of hospitalization can be used as an argument for or against the use of either procedure.

COMMENT

Which is the best procedure to use in the surgical treatment of pilonidal sinus? While it is true that this study is not comprehensive enough to evaluate all types of operative procedure, it appears that we have accumulated data which might be of value in revealing some of the important factors which should affect the choice of operation. There appears to be little doubt that the complications exclusive of recurrence are more numerous in the closed group. However, these become significant only if one can demonstrate that such complications prolong the length of time required for wound healing beyond that which might have been expected if the wound had originally been left open. In this series there is no such evidence. The average healing time for open wounds was 62.9 days. The average healing time for sutured wounds which were packed open because of infection was 63 days. Sutured wounds complicated by separation required an average of 33 days to heal completely. Lest it be argued that healing time might be expected to be longer in the open group because larger lesions are treated by this method, reference is made to Figure 3, which summarizes the amount of tissue removed in the various types of operation. It will be seen that there is little correlation between the amount of tissue removed and the type of operation. It must be admitted, therefore, that infection and separation are not serious complications if handled properly, and, therefore, their likelihood of occurrence should not prevent the surgeon from closing wounds, other factors being equal. Although

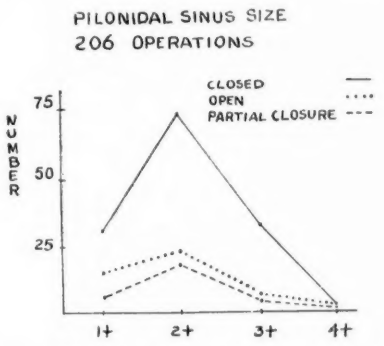

Fig. 3.—Pilonidal Sinus Size. Amount of tissue removed at time of operation correlated with closed, open or partial closure type of operation.

the incidence of recurrence in this series is slightly higher in the closed than in the open group, both figures are acceptably low. It is, indeed, doubtful that the difference is significant. It is probably true, as expressed by Dunphy,[10] that "more important than the method of treatment selected is the precision with which it is carried out." The varied results obtained by the various surgeons who performed the operations in this series would seem to support this statement.

SUMMARY AND CONCLUSION

Two hundred six operations performed by 20 surgeons are analyzed.

Complications are more frequent following closed operations, but these do not appear

to alter significantly the patient's ultimate postoperative results.

Both open and closed operations have their uses. Good results will be obtained with either operation provided it is carefully carried out.

REFERENCES

1. MacFee, W. F.: Pilonidal Cysts and Sinuses: A Method of Wound Closure; A Review of 230 Cases, Ann. Surg. **116**:687-699 (Jan.) 1942.

2. Rosser, C., and Kerr, J. G.: Pilonidal Disease: Present Status of Management, J. A. M. A. **133**:1003-1007 (April) 1947.

3. Brust, J. C. M., and Sarner, J. B.: Pilonidal Cyst, New York J. Med. **48**:2138-2144 (Oct.) 1948.

4. Liburt, J.: Pilonidal Cyst and Sinus, New England J. Med. **238**:806-808 (June 3) and 840-843 (June 10) 1948.

5. Palumbo, L. T.; Larimore, O. M., and Katz, I. A.: Pilonidal Cysts and Sinuses: A Statistical Review, A. M. A. Arch. Surg. **63**:852-857 (Dec.) 1951.

6. Lawrence, K. B., and Baker, W. J.: The Marsupialization Operation for Pilonidal Sinus: A Comparison with Other Surgical Methods in 359 Cases, New England J. Med. **245**:134-139 (July 26) 1951.

7. Holman, E.: Pilonidal Sinus: Treatment by Primary Closure, Surg., Gynec. & Obst. **83**: 94-100 (July) 1946.

8. Larkin, L. C.: Pilonidal Cyst: Analysis of 100 Consecutive Cases, Emphasizing Treatment by Radical Excision, Primary Closure and Penicillin Therapy, Surg., Gynec. & Obst. **82**:694-704 (June) 1946.

9. Pope, C., and Hudson, H. W.: Pilonidal Sinus: A Review of 130 Consecutive Cases in Which Patients Were Treated by Closure: A New Closed Operative Method and Management, Arch. Surg. **52**:690-700 (June) 1946.

10. Pope, C. E.: New and Successful Closed Operative Procedure for Pilonidal Sinus: Gluteus Maximus Mobilization; A Sliding Muscle Graft Procedure, Arch. Surg. **52**:701-712 (June) 1946.

11. Larsen, B. B.: Comparative Results in Operations for Pilonidal Cysts, Arch. Surg. **56**: 516-521 (April) 1948.

12. Firestone, E. O.: Technic of Excision and Primary Closure of Pilonidal Sinus, New York J. Med. **48**:2138-2144 (Oct. 1) 1948.

13. Harberson, J. C., and Brintnall, E. S.: Surgical Principles in the Treatment of Pilonidal Cyst and Its Complications, Am. J. Surg. **79**: 101-109 (Jan.) 1950.

14. Turell, R., and Gladstone, A. A.: Pilonidal (Sacrococcygeal) Sinus and Cyst, Internat. Abst. Surg. **93**:417-423, 1951; in Surg., Gynec. & Obst., June, 1951.

15. Gage, M.: Pilonidal Sinus: Sacrococcygeal Ectodermal Cysts and Sinuses, Ann. Surg. **109**: 291-303 (Feb.) 1939.

16. Rogers, H., and Hall, M. G.: Pilonidal Sinus: Surgical Treatment and Pathologic Structure, Arch. Surg. **31**:742-766 (Nov.) 1935.

17. Zieman, S. A.: Pilonidal Cysts, Surg., Gynec. & Obst. **66**:231-235 (Feb.) 1938.

18. Lahey, F. H.: A Further Suggestion for the Operative Treatment of Pilonidal Sinuses, Surg., Gynec. & Obst. **54**:521-523 (March) 1932.

19. Dunphy, J. E., and Matson, D. D.: The Treatment of Pilonidal Sinus, Surg., Gynec. & Obst. **75**:737-742 (March) 1942.

Sliding Hernias

A Follow-Up Study

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Sliding hernias of all inguinal ruptures are prone to cause the most difficulty at the time of repair and to have the highest incidence of recurrence. This tendency has influenced some surgeons to utilize a separate abdominal incision in an effort to achieve a more satisfactory repair. At the Veterans Administration Medical Teaching Group Hospital (Kennedy), Memphis, these hernias have been repaired almost exclusively through an inguinal incision. There is very little information in the literature regarding the incidence of recurrence following the combined incisional approach to sliding hernia, so that it is difficult to make any well-substantiated comparisons. A review of the cases at this hospital was undertaken to find out whether any change in technique might be indicated in view of the results.

Of first importance in such a study is a correct diagnosis at the operating table. Moschcowitz,[5] in 1925, stated with much discernment into human weakness that the commonest mistake is bravado on the part of the operating surgeon who calls any hernia which happens to have the colon as content a sliding hernia. Perhaps he feels that if the "tough slider" he struggled with recurs he will be absolved of blame. It is necessary, then, to define a sliding hernia. Bevan[1] agreed with Walton's[6] definition that a sliding hernia is one in which some portion of the wall is formed by a viscus which in its normal position is only partly covered by peritoneum. Moschcowitz[5] recognized that the mesosigmoid could become unfolded, and the sigmoid flexure might then become a sliding viscus. Each of Graham's[2] four cases occurred with the free sigmoid loop forming the apex of the hernia. A point of confusion arises when the cecum or sigmoid colon may apparently form part of the wall of the sac, when it is in reality merely attached to the wall by adhesions. If the bowel can be completely freed and returned to the abdomen while leaving an intact sac, the hernia is not a sliding one. Although hernias of the bladder are often considered to be sliding hernias, none was included in this study.

Of 1200 inguinal hernias repaired at this hospital up to two years ago, 75 were purported to be sliding. Fifty-nine of these 75 were considered to be bona fide cases, an incidence of 4.9% of all the inguinal hernias. Probably a few were discarded that were really sliding in nature for want of an accurate operative note to indicate what was done in management of the large bowel. Other cases were discarded in which it appeared that the large bowel was visualized only at the apex of the sac when strong traction was placed on the sac. In still others it was quite clear that the colon was adherent in the hernial sac. Those that were finally selected for review were well justified by the operative note and presented some problem in repair.

When the 59 cases were reviewed, it was found that 5 patients had died sometime after leaving the hospital of causes not related to hernia. One patient could not be located. The remaining 53 were examined personally by one or, more usually, several physicians. One patient was examined at

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the Veterans Administration Hospital in St. Louis, through the courtesy of Dr. Coldwater. If one of the physicians thought a recurrence was present, the case was counted as a recurrence.

The operations were performed from 1947 to 1952; all patients were seen for evaluation at least two years after operation. Hagan and Rhoads [8] have shown that in two years about 55% of the recurrences will have appeared. Among the 53 patients seven recurrent hernias were found. Two of these were large, and reoperation was performed. In two others the recurrence was small and not evident to the patient. In the remaining three patients, the recurrence was so small that not all the examining physicians agreed that it was present. It was in the nature of a small impulse at the external inguinal ring,

Results of Follow-Up Examination After Operation for Sliding Hernia

Total cases		53
Large recurrence	2	
Small recurrence	2	
Questionable recurrence	3	
Total recurrence	7	
Per cent recurrence		13

found only with difficulty and "squashy" to touch. One of our examining physicians termed this a "fluff sign." The inguinal rings of these patients were all felt to be smaller than the end of the fifth finger. It will be interesting to determine whether these patients with a small questionable recurrence later develop a clinically important one. The results are listed in the Table.

One operation was performed in 1947, and this patient developed one of the small questionable recurrences. After the four operations performed in 1948, no recurrence developed. Nine hernias were repaired in 1949 and one recurred. This patient was found to have a fluff sign. The seven herniorrhaphies done in 1950 were followed by one large recurrence which developed six months after surgery, when the patient resumed hard work. Fifteen hernias were repaired in 1951. There were three recurrences, two being small and one being very small and recognized by the fluff sign. Nineteen hernias were repaired in 1952 with one recurrence, a very large one, which appeared three months postoperatively.

It is said [7] that the presence of sliding hernia should be suspected when a hernia is impossible to reduce completely, is difficult to control by pressure, and has a large defect at the internal ring. The correct diagnosis was suspected preoperatively in four of the cases in this series. Colonography was not used as an aid in the diagnosis of sliding hernia. All hernias were reducible preoperatively. In four instances, mention was made that a truss was tried but could not be tolerated.

The age of one patient was in the decade 20 to 29, eight in the decade 30 to 39, three in the decade 40 to 49, thirty-three in the decade 50 to 59, six in the decade 60 to 69, and two in the decade 70 to 79. Of the patients with large recurrences, one was 59 and the other 55 years of age. The patients with the smaller recurrences had been operated on at ages 64, 56, 57, 44, and 39.

Of the hernias, 37 were on the left and 16 on the right. One of the large recurrences was on the right; all others were on the left.

The duration of the hernias varied from 6 months to 47 years, with an average of 10 years. In the cases of large recurrence the preoperative duration was 1 year in one and 32 years in the other, while in the small recurrences the preoperative duration averaged 6 years. Certainly recurrence was not necessarily associated with long preoperative duration of hernia.

We performed most of the repairs using a high ligation of the sac, carrying the dissection as high as the bladder, and using a 0 nonabsorbable surgical (silk) purse-string suture to close the sac. All hernias were indirect save two recurrent hernias which presented medial to the inferior deep epigastric vessels. By and large, the repairs were Halsted in type using 00 nonabsorbable surgical silk when suturing the conjoined tendon to the inguinal ligament. In one patient with a large recurrence 0 nonabsorb-

able surgical silk had been used, and in one with small recurrence 000 silk had been used. In one patient with a small recurrence a McVay repair with a subcutaneous transplantation of the cord had been utilized. All other recurrences took place after Halsted repairs .The Bassini repair was used 10 times and the McVay repair 7 times. The use of the Bassini repair was not confined to the younger age group.

The policy in repair was predominantly the reperitonealization of the mesentery of the bowel by bottling a peritoneal leaf behind the bowel. It was found that in many cases this could very satisfactorily be done, although in cases of sacless hernia this was not accomplished. All operations were done from the inguinal approach alone except two. In one instance the visceral and parietal peritoneum were fused by extensive filmy adhesions, the only free peritoneal cavity being found in the region of the stomach. It was thought that this patient had had tuberculous peritonitis, and there developed clinical evidence of reactivation early in 1954, five years after the operation. In another instance, no sac was present on the left, the large bowel presenting into the incision. A LaRoque [4] approach was used. In this patient, who was a severe cardiac, local anesthesia was employed. Even with the additional abdominal incision, the operator did not feel that he had achieved a satisfactory reduction of the sigmoid in this sacless hernia. Even though the operator thought that the possibility of recurrence was great, there has not been one in more than two years.

No deaths resulted from the 53 operations. In the case of one of the two large recurrences reoperation was undertaken in March, 1954. This patient died about 75 minutes postoperatively, evidently of a cardiac arrest related to anesthetic drugs. The autopsy disclosed no cause of death. The postmortem examination did, however, permit an evaluation of the effectiveness of the reduction of the large bowel, which had been accomplished in this large hernia through the inguinal approach. The mesentery of the sigmoid had been completely re-formed, and the bowel lay intraperitoneally well away from the internal ring, thus demonstrating the feasibility of completely reperitonealizing the mesentery of the sigmoid in this large parasaccular hernia without the use of a laparotomy incision. In 25 cases of this series, the mesentery was reperitonealized. It was accomplished in one of the two large recurrences and in three of the five small recurrences. Zimmerman and Laufman [8] maintained that bottling of the bowel is not necessary. Our figures do not show a high recurrence in cases in which this was not done, but it would appear desirable, since this maneuver permits the bowel to lie intraperitoneally away from the internal ring.

Orchiectomy was performed five times. The blood supply to the testis was compromised during the dissection prior to three of the orchiectomies. One of these patients had a herniorrhaphy on the opposite side for a nonsliding hernia and developed atrophy of the remaining testis. He was 58. In two additional patients, ages 73 and 75, the testis was removed in order to obtain a better repair. Our policy is not to perform orchiectomy as a general rule. This attitude is especially justified in a patient with bilateral hernia. Two patients developed atrophy of the testis after a sliding-hernia repair. Three patients developed hydroceles postoperatively. In none of the recurrences did prostatism or constipation play a part. One patient with a small recurrence had had a chronic cough for several years prior to herniorrhaphy. One patient with pulmonary tuberculosis underwent herniorrhaphy six weeks prior to pneumoperitoneum. This patient has not developed a recurrence.

Infection occurred in two wounds. In both patients later incision with removal of sutures became necessary. In neither instance did recurrence develop. The culture from one wound revealed hemolytic Staphylococcus aureus, and from the other a nonhemolytic Staph. aureus was grown. The patients were routinely given penicillin postoperatively.

Appendectomy was performed five times. In all five the appendix was removed because it either formed part of the lateral wall of the sac or interfered with a proper high ligation of the sac. One of the infections occurred in the appendectomy group.

Spinal anesthesia was used 32 times, inhalation anesthesia 13 times, and local anesthesia 8 times. One of the large recurrences and four of the small recurrences followed operations under spinal anesthesia. The second large recurrence followed operation under inhalation, and one small recurrence followed operation under local anesthesia. Local anesthesia was used for large as well as small hernias and was employed in six cases because of heart disease, in one because of chronic bronchitis, and in one because of advanced age.

An insufficient number of operations were done by any one surgeon to provide significant figures regarding their recurrence rate, but one surgeon operated six times, with three recurrences. One of these was large and two were small. One surgeon operated twice, with one large recurrence; one three times, with one small recurrence; one four times, with one small recurrence, and one six times, with one small recurrence. No other surgeon operated more than three times. Thus, two surgeons operated seven times and had four-sevenths of the recurrences in the 53 cases. Although these figures do not have any statistical significance, they are not at variance with the concept that the surgeon himself is more important than the particular method he uses.

Consideration of inguinal hernias of any type on the opposite side in these patients revealed some interesting findings. In one patient a hernia which had been repaired on the side opposite the sliding hernia one and one-half years previously recurred as a small sliding hernia. The repair on this recurrent hernia is not one of the repairs included in this report, since it was performed recently. The original description was detailed and conveys the impression that this hernia was not one which had been misdiagnosed as nonsliding at the first operation. Perhaps the high sac ligation predisposed to its recurrence as a sliding hernia. Twenty-six patients had a hernia on the other side at some time. Twelve repairs were performed at the hospital prior to 1953. Of these, two recurred, or an incidence of 17% of nonsliding hernias. This high incidence of recurrence of the nonsliding type is probably not characteristic of the larger group repaired at this hospital, but it is a higher incidence than that found in the sliding-hernia group when one might well expect the opposite to be true. Our policy is not to perform bilateral herniorrhaphies at the same time. The operator may hurry unduly on the second side, and on this side there will be less tension if the operation is carried out about a week later.

Ten of the 53 patients had recurrent hernias at the time we operated. One patient was three times recurrent when admitted to this hospital. No further recurrences followed the repair in these patients. One of the recurrent sliding hernias had been repaired at this hospital two years previously. The operative note was detailed and mentioned that a high ligation of the sac had been accomplished. There was no evidence that this hernia had been unrecognized as a sliding hernia at that first repair. In two cases only the area of recurrence was repaired. The other recurrences were so large that the entire repair was redone. Our present policy in any recurrent hernia is to take down only that portion of the hernia repair that is necessary for achievement of a strong closure.

COMMENT

In any sliding hernia it is important to make an accurate diagnosis at the operating table and to make a full and complete operative report so that no question can arise to confuse the figures when these cases are later studied. It is essential that any follow-up reports be made on the basis of personal examination by physicians, since in five of the seven recurrences the patients had no knowledge of a recurrence. It was found that a satisfactory restoration of the

peritoneal relations could be achieved in the parasaccular hernias, and in the sacless hernias a satisfactory reperitonealization could not be done, even though a LaRoque incision was made in one of these. Despite this, there was no greater incidence of recurrence when the reperitonealization was not accomplished. By and large, the policy was not to perform orchiectomy. The surgeon is probably more important than the particular method he uses. No further recurrence was observed after 10 operations for recurrent hernia.

SUMMARY

Fifty-three cases of sliding hernia seen on follow-up examination at least two years after operation are reviewed. There were two large recurrences, two small ones, and three questionable ones which may prove to be significant in later years.

The inguinal approach proved to be feasible and yielded a sufficiently low recurrence rate that it is not felt justified to recommend a concomitant abdominal incision with its greater morbidity, especially in the absence of any indication that a lower recurrence rate would result.

REFERENCES

1. Bevan, A. D.: Sliding Hernias of the Ascending Colon and Caecum, the Descending Colon and Sigmoid, and of the Bladder, Ann. Surg. **92**:754, 1930.

2. Graham, R. R.: Operative Repair of Sliding Hernia of Sigmoid, Ann. Surg. **102**:784, 1935.

3. Hagan, W. H., and Rhoads, J. E.: Inguinal and Femoral Hernias: A Follow-Up Study, Surg., Gynec. & Obst. **96**:226, 1953.

4. LaRoque, G. P.: Intra-Abdominal Method of Removing Inguinal and Femoral Hernia, Arch. Surg. **24**:189, 1932.

5. Moschcowitz, A. V.: Rational Treatment of Sliding Hernia, Ann. Surg. **81**:330, 1925.

6. Walton, A. J.: Extrasaccular Hernia, Ann. Surg. **57**:86, 1913.

7. Williams, C.: Repair of Sliding Inguinal Hernia Through Abdominal (LaRoque) Approach, Ann. Surg. **126**:612, 1947.

8. Zimmerman, L. M., and Laufman, H.: Sliding Hernia, Surg., Gynec. & Obst. **75**:76, 1942.

Benign Tumors of the Small Intestine

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Nearly one of every four benign tumors of the gastrointestinal tract is found in the small intestine.[1] However, only between 9 and 16 times in every 10,000 autopsies and/or biopsies will a benign tumor of the small bowel be discovered (Table 1). This disproportion between the frequency of neoplasia and great length (as compared with the relatively short large intestine) has been attributed to various factors, including the following: (1) lack of irritation owing to the absence of stasis associated with the speed of passage of fecal content. Neoplasms arise most frequently in the duodenum and ileum and less frequently in the jejunum; (2) the infrequent presence of embryonal rests here as compared with other portions of the alimentary tract.

The small bowel is approximately 23 ft. long, with extreme variations from about 15 ft. to about 32 ft.[2] Any histological element of this huge area is subject to neoplastic overdevelopment, but certain cellular entities seem more susceptible than others. Thus, adenomas constitute about one-third of the benign tumors of this region, followed by myomas and, last, by fibromas, lipomas, and pancreatic rests.[3] Olson, Dockerty and Gray[4] list 10 different types of tumors: adenoma, leiomyoma, fibroma, lipoma, accessory pancreatic rests, hemangioma, cysts, lymphangioma, hematoma, and osteochondroma. To these may be added neurofibroma (from material seen at Cumberland Hospital) and melanoma. Carcinoids (argentaffin tumors) are not included in this group. In view of their high incidence of metastasis, the opinion is rapidly coming to the fore that they must be considered to be malignant neoplasms, although of low grade nature.[5]

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TABLE 1.—*Frequency of Benign Tumors of the Small Intestine*

Author	Tumors, No.	Source: Autopsies	Source: Surgical Specimens	Per Cent
Ralford [1]	50	11,500	45,000	0.09
Buckstein [37]	88	56,000	.....	0.16
Morison [38]	13	2,434	10,705	0.10
Shandalow (this series)	22	2,648	.....	0.83

TABLE 2.—*Ratio of Benign and Malignant Tumors of the Small Intestine*

Source	Cases, No.	Benign %	Benign No.	Malignant %	Malignant No.
Morison [38]	17	77	13	23	4
Dundon [39]	62	77	44	29	18
Ralford [1]	88	57.8	51	42.2	37
Eckel [16]	19	37	7	63	12
Shandalow (this series)	25	88	22	12	3

SOURCE MATERIAL

At the Cumberland Hospital, in Brooklyn, 2648 autopsies were performed between February, 1940, and April, 1954. A total of 25 tumors of the small intestine were discovered, of which 88% (22) were benign and 12% (3) were malignant. This ratio of nonmalignant growths is higher than in other published statistics (Table 2). Of the 22 benign tumors (Table 3), 32% (7) were located in the duodenum; 32% (7), in the jejunum, and 22% (3), in the ileum. Three tumors (14%) were multiple and were situated in the duodenum, jejunum, and ileum. The following neoplasms were encountered: adenomas, 6; myomas, 3; lipomas, 2; neurofibromas, 3; hemangiomas, 4; aberrant pancreas, 1; lymphatic cysts, 2, and fibroma, 1. The relative high incidence (0.83%) of benign tumors in this series (Table 1), which is four to nine times higher than that in other published figures, may probably be attributed to the careful postmortem examination of every inch of the intestinal tract, a procedure which is not generally followed in autopsies elsewhere.

TABLE 3.—*Benign Tumors of the Small Intestines in 2648 Autopsies at Cumberland Hospital, February, 1940, to April, 1954*

Case No.	Type	Location	Age, Yr.	Sex	Race	Size, Cm.	Symptoms Phys. Find., X-Ray Find.	Date
1	Adenoma	Ileum	54	F	W	0.5	0	6/18/40
2	Adenoma	Ileum	63	M	W	1.0	0	7/ 9/49
3	Adenoma	Duodenum	88	F	W	5.0 multiple	0	8/14/51
4	Adenoma	Duodenum	34	M	N	0.3	0	4/28/52
5	Adenoma	Jejunum	57	M	N	1.0	0	8/22/45
6	Adenoma	Duodenum	50	M	N	...	0	10/26/53
7	Leiomyoma	Duodenum	80	M	W	4.0	0	9/29/39
8	Fibromyoma	Jejunum	80	F	W	0.5	0	1/13/44
9	Fibromyoma	Ileum	59	F	W	...	0	9/23/49
10	Fibroma	Jejunum	75	M	W	1.3	0	3/ 8/45
11	Lipoma	Jejunum	38	M	W	1.0	0	10/23/49
12	Lipoma	Duodenum	75	F	W	1.0	0	6/22/45
13	Neurofibroma	Ileum	65	M	N	0.7	0	7/18/42
14	Neurofibroma	Duodenum	75	M	W	1.5	0	3/15/45
15	Neurofibroma	Jejunum	39	M	N	...	0	6/23/48
16	Hemangioma	Jejunum	63	M	W	0.4	0	5/ 9/47
17	Hemangioma	Duodenum (ampulla of Vater)	73	F	N	...	0	8/ 3/43
18	Hemangioma	Multiple	65	M	W	...	0	6/19/45
19	Hemangioma	Multiple	39	M	..	...	0	6/25/45
20	Aberrant pancreas	Jejunum	54	F	N	...	0	6/20/49
21	Lymphatic cyst	Multiple	63	M	W	0.6	0	2/16/40
22	Lymphatic cyst	Ileum	77	M	W	1.0	0	2/15/41

ADENOMA

Adenomas, which are the commonest benign tumors of the small intestine, constituting about one-third of all benign growths in this location, are situated most frequently in the duodenum and ileum and rarely in the jejunum.[3] Almost two of every three are found in the ileum.[1] Six adenomas were found at autopsy at Cumberland Hospital. Three were in the duodenum; one was in the jejunum; and two were in the ileum—the total representing six of twenty-two, or 27% of the benign tumors in this series.

Grossly these neoplasms are recognized as hyperemic polypoid masses, deep red, with an intact mucosal surface. They are usually single,[6] ranging in size from 1 mm. to several centimeters. In the duodenum the adenoma is more likely to be of the sessile variety.

Clinically adenomas are of little importance. Their infrequent complications include bleeding, malignant change (rarely), bowel obstruction, and intussusception (as peristalsis may propel even a small tumor into the distal bowel segment).

MYOMA

The incidence of myomas of the small intestine is very low. Chont[7] examined 20,003 surgical specimens removed from the small bowel and discovered only 3 leiomyomas. Yet, myomas are second only to adenomas in frequency of occurrence in the small intestine. They are much more important, however, from a clinical and surgical viewpoint. Like adenomas, myomas are commonest in the ileum, but, unlike adenomas, their next greatest predilection is for the jejunum.[8]

The small submucous or intraluminal myomas may cause intussusception or intestinal obstruction and may give rise to extensive hemorrhage. Barb[9] described a case in which a jejunal leiomyoma simulated, both clinically and radiographically, a bleeding peptic ulcer. Hanno and Mensh[8] reported a case of intermittent melena of 14 years' duration followed by fatal hemorrhage. On the other hand, the large subserous or extraluminal smooth muscle tumors which encroach upon the peritoneal cavity may reach a size at which central necrosis, per-

foration, and malignant degeneration may occur. Bockus [10] reported the incidence of metastases following sarcomatous change in extraluminal myomas as one in six (16%). Klopp and Crawford [11] set this figure as high as one in five (20%). Lumb,[12] on the other hand, advanced the thesis that metastasis is a rare event which, however, does occur from time to time. Ewing [13] did not conform entirely to the belief that it is possible for benign myomas to develop into malignant tumors. He stated: "It is not to be assumed that malignant myomas represent transformation of previously benign tumors. Many and probably all these tumors are *malignant from the start.*" *

The present series comprises 3 myomas in a total of 22 benign tumors (13.6%).

TABLE 4.—*Location of Lipomas of the Small Intestine*

Source	Total Cases	Duodenum, %	Jejunum, %	Ileum, %
Comfort [40]	58	22.4	19	58.6
Smith and Mayo [41]	67	33	25	42
Schottenfeld [15]	16	*	*	43.8

* Not given.

These were situated as follows: leiomyoma of duodenum, 1; myofibroma of jejunum, 1; myofibroma of ileum, 1. None had produced recognizable symptoms during the life of the patient.

LIPOMA

Lipomas of the small intestine are rare tumors. In 38,741 autopsies Schottenfeld [15] found only 16 lipomas (0.04%). In the present series, while the incidence was almost double that just cited, namely, two lipomas in 2648 autopsies (0.076%), their frequency is still very low. Yet lipomas rank third among all the benign tumors of the small bowel, exceeded only by adenomas and myomas. Raiford,[1] for example, found 7 lipomas among 50 benign tumors of this region (14%), which figure corresponds well with the experience of Eckel.[16] In the present series there were only two lipomas among the 22 benign tumors reported, giving a much lower percentage (9%). Most lipomas are discovered in the ileum, this region being the site in 40% to 60% of all cases (Table 4).

On examination of the intestinal wall, lipomas are identified as yellowish soft sessile or polypoid masses, 85% of which are intraluminal. These noninvasive tumors may be single or multiple, as small as a few millimeters or as large as an orange. Roan,[17] who studied 100 cases of intussusception attributable to benign tumors of the small intestine, came to the conclusion that lipomas were the cause in 11% of the cases. Ulcerated duodenal lipomas may mimic the peptic ulcer syndrome.

As has been previously stated, two lipomas were discovered in 2648 autopsies at Cumberland Hospital. In both instances they were asymptomatic and incidental findings.

FIBROMA

True fibromas of the small intestine, containing no admixture of other cellular elements, are rare. Cases reported as fibroadenoma, fibromyoma, or fibromyxoma cannot be considered as actual fibromas.

Moore and Schmeisser [14] reviewed 42 cases of fibroma in the literature up to 1937. Of those whose location was given (32 cases), 23 (72%) were in the ileum; 6 (19%) were in the jejunum, and 3 (9%) were in the duodenum. The predilection of these growths for the ileum is confirmed by Raiford.[1]

Clinically, there have been cases of intussusception in which an intraluminal fibroma could be indicted as the causative agent. In the main, however, they are asymptomatic.

In our series of 22 cases only 1 true fibroma was encountered. This was an accidental discovery during the postmortem examination of a 75-year-old white man. The tumor was situated in the jejunum and measured 1.3 cm.

There seems to be no age or sex specificity. Fibromas have been found in patients as young as 8 and as old as 66 years.

* Author's italics.

While intraluminal growths predominate, extraluminal fibromas may attain the size of an adult head. They may be present in the mesentery or retroperitoneally or may detach themselves and appear free in the peritoneal cavity as firm, rubbery, grayish-white masses. Intraluminal neoplasms of this type may be pedunculated or sessile, with an intact overlying mucosa or with a mucous covering which is ulcerated and bleeding. Combination forms may be mistaken for malignant tumors, being both enteric and exoenteric irregular masses invading both the lumen and the peritoneal space.

NEUROFIBROMA

In 1944 Bockus [10] collected a total of nine cases of neurogenic tumors of the small bowel which had been reported in the literature to that date. The present series adds 3 neurofibromas to the existing literature, making a total of 12 cases.

Neurogenic tumors may originate along the course of the autonomic fibers where ganglion cells are found, as in the plexus of Meissner and Auerbach in the intestine,[18] especially in the ileum. They may be single or multiple, sessile or pedunculated, and of variable sizes, and they resemble the fibromas in consistency and shape. Occasionally, when the tumor is irregular and has both intraluminal and extraserosal projections, it may be mistaken for carcinoma on gross inspection. While most neurofibromas are silent, as in our own three cases, they may occasionally be the source of massive intestinal hemorrhage. Baker and Halley [19] reported two such instances in 1946. Both growths were pedunculated.

HEMANGIOMA

Hemangiomas constitute about 6% of all benign tumors and 8.4% of all varieties of tumors of the small intestine.[20] By 1942 Christopher [21] had collected 11 more cases of hemangioma of this location, which, added to Kaijser's 74,[22] made a total of 85.

They are usually single intraluminal growths, but in more than one-third [23] of the examples in the literature they are multiple, being scattered throughout the small intestine and frequently associated with similar lesions of the colon or of the entire gastrointestinal tract. In our series of 22 cases of benign small bowel neoplasms, we list 4 additional instances of hemangioma, 2 of which (50%) were multiple. There is no age or sex specificity.

During surgery or on postmortem examination, hemangiomas are recognizable as small reddish submucous nodules covered by a mucosa which is seldom broken but is markedly hyperemic.

Clinically, ulceration of these neoplasms is one of the principal causes of obscure intestinal hemorrhage with resulting melena. When the tumor protrudes beyond the serosa, massive bleeding may occur retroperitoneally or into the mesentery. According to their location, they may simulate to a confusing degree the symptoms of ulcer (in the duodenum) or of ulcerative colitis (in the ileum). Lichtenstein and Dutra [23] described a case of intussusception in 1943 traced to an angiofibroma of the ileum.

It is of interest to note that one of our hemangiomas was situated in the duodenum at the ampulla of Vater. Yet no obstructive symptoms were observed during life, and the lesion was asymptomatic. Had this patient developed jaundice, one could speculate as to whether the surgeon would have even considered the possibility of a benign vascular growth as the etiologic factor.

ABERRANT PANCREAS

Aberrant pancreatic tissue is merely normal pancreatic tissue abnormally situated. In the small intestine, the favorite sites are the duodenum, ileum, and Meckel's diverticulum, and such tissue is least often situated in the jejunum. Horsley and Keasbey [24] collected 328 cases of heterotopic pancreatic rests. In our series at Cumberland Hospital we came across only one, located in its least frequent situation, the jejunum. Revealed only at autopsy, it had previously been asymptomatic.

Pancreatic rests can be seen in the submucosa, varying in size from minute nodules to masses up to 10 cm. in diameter. They are symptomless, as a rule.

Grossly, duodenal aberrant pancreatic accumulations have been mistaken for carcinoma, but their relation to malignant lesions is still in doubt. Duff, Foster, and Bryan [25] postulate that aberrant pancreas tissue may undergo malignant transformation, and they cite a case of primary carcinoma of the infraampullary portion of the duodenum which, they believe, originated in this manner.

In our 2648 autopsies only 1 instance of aberrant pancreatic rest was revealed. Here the abnormality was in the jejunum and had been completely silent.

INTESTINAL CYSTS

This classification includes lymphatic cysts, with which variety we are particularly concerned. At Cumberland Hospital, out of a total of 22 benign neoplasms, 2 lymphatic cysts (9%) were discovered during routine necropsy. Both patients were white men, one 63, the other 77. This is of interest in view of the rarity of these tumors and also in relation to Bockus' experience [10] that these cysts occur most frequently in infants and children. Raiford [1] found only 1 lymphatic cyst in his series of 88 benign growths of the small intestine (1.1%).

Cysts of the small intestine are solitary or multiple, occurring mostly as extraluminal extensions from the intestine. They may be very small or may resemble an ovarian cyst in size and consistency during a bimanual pelvic examination. Lymphatic cysts may be located anywhere in the small intestine or in the adjacent mesentery but are most frequently encountered in the ileum. They contain a fluid which may be clear, milky, or bloody.

Gas cysts, which are occasionally found in the region under discussion, were not met with in our series at Cumberland Hospital. Also known as cystic pneumatoses, they consist of subserosal grape-like sterile gas collections under the intestinal peritoneum, from minute bubbles to balloon-like masses. Moore [26] explains their formation by the entrance of intestinal gas into the lymphatics through a break in the mucosa or at the site of an ulcer.

Intestinal cysts, being rare and usually small, are of little clinical importance.

MELANOMA

In most cases intestinal melanoma is secondary to nevi of the skin or to melanoma of the retina or rectum. Another but generally unrecognized, primary source, suggested by Herbut and Manges,[27] is the mongol cells (true melanoblasts), which lie deep in the corium over the sacrum and along the back in infants of all races.

In 1936 Menne and Beeman [28] collected, in a review of the literature, eight cases of melanoma of the small intestine in which no other primary focus could be found. In 1941 Gordon [29] added one other such tumor, which he designated as primary because of the apparent absence of an original focus elsewhere. However, he questioned the spontaneous development of melanoma in the intestine.

No melanomas were found in the autopsies forming the basis for this report.

DIAGNOSIS

At the outset it must be reiterated that benign tumors of the small intestine are infrequent and usually asymptomatic and that they are found mostly as incidental discoveries at the autopsy table. The various complications attributable to these neoplasms are (1) hemorrhage either into the intestinal lumen or into the peritoneal cavity; (2) intestinal obstruction; (3) intussusception; (4) ulceration, causing pain and irritability; (5) malignant degeneration.

The commoner known causes of these sequelae must first be excluded. Then only should measures be taken to rule out benign tumors of the small intestine as possible etiological factors. The most valuable of these procedures are serial x-ray studies of the small bowel, with the barium introduced orally or by direct intubation of the duodenum. Occasionally, obscure cases of per-

sistent anemia or recurrent anorexia or vomiting can be explained on the basis of demonstrable ulcerated or obstructing small intestine growths.

TREATMENT AND PROGNOSIS

After detection of the location of what is believed to be a benign tumor by roentgen studies or during an exploratory laparotomy for persistent melena or obstruction of the small bowel, the involved segment should be opened. A small nonmalignant tumor may be excised together with that portion of the wall to which it is affixed. If the neoplasm is at all suggestive of malignant transformation, biopsy and immediate examination of the frozen section are indicated. A serious situation confronts the surgeon who has discovered that he is dealing with a benign growth in which malignant transformation has supervened. That he must submit the patient to radical surgery just as he would in the case of any other malignant growth is unquestioned. The presence of regional metastases and the degree of infiltration of adjacent or contiguous loops of intestine or other structures must determine the extent of the surgical procedure. Massive resection of the small bowel may be imperative and has been performed many times, with survival of the patient.† In one case in 1950 Shonyo and Jackson [32] excised all but 3.5 in. of jejunum and 1 in. of ileum. Malnutrition, weakness, intractable diarrhea, and difficulty in maintaining fluid balance are the principal undesirable sequelae.

Differentiation from carcinoma becomes difficult when there is considerable metaplasia in an otherwise benign adenoma. In these cases Foot [36] advises excision of the mass. If no invasion of the pedicle is found, he considers it only locally malignant and does not proceed with further, more radical, surgery.

While malignant involvement of many loops is the most likely reason for resection of large portions of the small intestine, persistent bleeding from multiple hemangiomas or even ulcerated neurofibromatosis may conceivably require similar extensive resection.

SUMMARY AND CONCLUSIONS

At the Cumberland Hospital 22 benign tumors were encountered in 2648 consecutive autopsies performed between 1940 and 1954. This ratio (0.83%) is four to nine times higher than that usually reported (0.09% to 0.16%) and may possibly be due to a more careful inspection of the small bowel during routine postmortem examination. In all our cases the tumors were entirely symptomless, did not contribute to death, and were discovered as incidental findings. They included six adenomas, three myomas, two lipomas, one fibroma, three neurofibromas, four hemangiomas, one aberrant pancreatic rest, and two lymphatic cysts.

Adenomas are usually the most frequent, followed by myomas and lipomas.

The sites of predilection are the duodenum and ileum, the jejunum being the least favored.

Infrequently, benign growths of the small intestine may account for obscure bleeding, obstruction, or intussusception and may undergo malignant degeneration. These possibilities must be considered whenever the usual causes of these syndromes cannot be demonstrated.

The treatment of uncomplicated benign neoplasms of the small intestine is simple, and the prognosis is favorable. On the other hand, the surgical management and prognosis of complicated growths consist, in effect, of the management and prognosis of intestinal hemorrhage (both intraluminal and intraperitoneal), of intestinal obstruction, of intussusception, and of the sequelae of malignant degeneration.

REFERENCES

1. Raiford T. S.: Tumors of the Small Intestine, Arch. Surg. **25**:122; 321, 1932.

2. Gray, H.: Anatomy of the Human Body, edited by C. M. Goss, Ed. 25, Philadelphia, Lea & Febiger, 1948, p. 1213.

3. Rankin, F. W., and Newell, C. E.: Benign Tumors of the Small Intestine: Report of 24 Cases, Surg., Gynec. & Obst. **57**:501, 1933.

† References 30 to 35.

4. Olson, J. B.; Dockerty, M. B., and Gray, H. K.: Benign Tumors of the Small Bowel, Ann. Surg. **134**:195, 1931.

5. Pearson, C. M., and Fitzgerald, P. J.: Carcinoid Tumors: A Re-Emphasis of Their Malignant Nature, Cancer **2**:1005, 1949.

6. Aird, I.: Tumors of the Small Intestine, in Carling, E. R., and Ross, J. P., Editors: British Surgical Practice, St. Louis, C. V. Mosby Company, 1948, Vol. 5, p. 540.

7. Chont, L. K.: Sarcomas of the Small Intestine and Reference to Their Radiosensitivity, Radiology **36**:86, 1941.

8. Hanno, H. A., and Mensh, M.: Leiomyoma of the Jejunum: Intermittent Melena of 14 Years' Duration and Fatal Hemorrhage, Ann. Surg. **120**:198, 1944.

9. Barb, J. S.: Jejunal Tumor Simulating Bleeding Duodenal Ulcer, New York J. Med. **54**:2097, 1954.

10. Bockus, H. L.: Tumors of the Small Intestine, in Gastro-Enterology, Philadelphia, W. B. Saunders Company, 1944, Vol. 2, Chap. 49, p. 124.

11. Klopp, E. J., and Crawford, B. L.: Leiomyoma of the Small Intestine, Ann. Surg. **101**:726, 1935.

12. Lumb, G.: Smooth Muscle Tumors of the Gastrointestinal Tract and the Retroperitoneal Tissues Presenting a Large Cystic Mass, J. Path. & Bact. **63**:139, 1931.

13. Ewing, J.: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1922.

14. Moore, R. M., and Schmeisser, H. C.: Benign Tumors of the Small Intestine, South. M. J. **27**:386, 1937.

15. Schottenfeld, L. E.: Lipomas of the Gastrointestinal Tract, Surgery **14**:47, 1943.

16. Eckel, J. H.: Primary Tumors of the Jejunum and Ileum, Surgery **23**:467, 1948.

17. Roan, O.: Intussusception Due to Benign Tumors of the Small Intestine, Texas J. Med. **27**:872, 1932.

18. Ritter, S. A.: Neuroblastoma of the Intestine, Am. J. Path. **1**:519, 1925.

19. Baker, H. L., and Halley, H.: Neurofibroma of the Small Intestine with Massive Hemorrhage, Ann. Surg. **123**:1067, 1946.

20. Hansen, P. S.: Hemangioma of the Small Intestine with Special Reference to Intussusception, Am. J. Clin. Path. **18**:14, 1948.

21. Christopher, G.: Hemangioma of the Ileum, Ann. Surg. **116**:945, 1942.

22. Kaijser, R.: Über Hämangiome des Tractus gastrointestinalis, Arch. klin. Chir. **187**:251, 1937.

23. Lichtenstein, M. E., and Dutra, F. R.: Angiofibroma of the Ileum, Arch. Surg. **47**:69, 1943.

24. Horsley, J. S., and Keasbey, L. E.: Tumors of the Small Intestines, in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1939, Vol. 4, Chap. 17.

25. Duff, G. L.; Foster, H. L., and Bryan, W. W.: Primary Carcinoma of the Infra-Ampullary Portion of the Duodenum, Arch. Surg. **46**:494, 1943.

26. Moore, R. A.: Intestinal Pneumatosis, Am. J. Dis. Child. **38**:818, 1929.

27. Herbut, P. A., and Manges, W. E.: Melanoma of the Small Intestine, Arch. Path. **39**:22, 1945.

28. Menne, F. R., and Beeman, J. A. P.: Multiple Primary Melanomas of the Small Intestine, Am. J. Digest. Dis. **3**:786, 1936.

29. Gordon, W. C.: Primary Melanoma of the Small Intestine with Report of a Case, Rev. Gastroenterol. **8**:36, 1941.

30. Berman L. G.; Ulevitch, H.; Haft, H. H., and Lemish, S.: Metabolic Studies of an Unusual Case of Survival Following Resection of All but 18 Inches of the Small Intestine Complicated by Combined Abdominoperineal Resection for Carcinoma of Rectum Performed 9 Years Previously, Ann. Surg. **132**:64, 1950.

31. Meyer, H. W.: Acute Superior Mesenteric Artery Thrombosis, Arch. Surg. **53**:298, 1946.

32. Shonyo, E. S., and Jackson, J. A.: Massive Resection of the Small Intestine, Arch. Surg. **61**:123, 1950.

33. Best, C. H., and Taylor, N. B.: Physiological Basis of Medical Practice, Ed. 5, Baltimore, Williams & Wilkins Company, 1950, Chap. 44, p. 579.

34. Linder, A. M.; Jackson, W. P. U., and Linder, G. C.: Small Gut Insufficiency Following Intestinal Surgery, South African J. Clin. Sc. **4**:1, 1953.

35. Pearce, A. E.; Entine, J. H., and Eksterowicz, F. C.: Massive Intestinal Resection with Survival, J. Internat. Coll. Surgeons **20**:322, 1953.

36. Foot, N. C.: Pathology in Surgery, Philadelphia, J. B. Lippincott Company, 1945, Chap. 12, p. 226.

37. Buckstein, J.: Clinical Roentgenology of the Alimentary Tract, Philadelphia, W. B. Saunders Company, 1940, p. 359.

38. Morison, J. E.: Tumors of the Small Intestine, Brit. J. Surg. **29**:139, 1941.

39. Dundon, C. C.: Primary Tumors of the Small Intestine, Am. J. Roentgenol. **59**:492, 1948.

40. Comfort, M. W.: Submucous Lipomata of the Gastro-Intestinal Tract, Surg., Gynec. & Obst. **52**:101, 1931.

41. Smith, F. R., and Mayo, C. W.: Submucous Lipomas of the Small Intestine, Am. J. Surg. **80**:922, 1950.

Surgical Treatment of Ruptured Aortic Aneurysms

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During the past few years excisional therapy of aortic aneurysms has been firmly established as the treatment of choice. The hazards of aortic aneurysms are well recognized. Thoracic aneurysms may cause unbearable pain from root compression and vertebral erosion. They may obstruct adjacent structures, such as trachea, bronchi, and esophagus. Abdominal aneurysms may also cause root pain. They sometimes bring about gastrointestinal dysfunction, and they may result in obstruction of the ureters or vesicle neck. The greatest hazard of aortic aneurysms, however, is rupture, and it is the threat of rupture which provides the single most compelling reason for advocating surgical treatment. When this complication occurs the patient is almost sure to die unless definitive surgery is carried out immediately. That prompt operation offers hope under such circumstances has been pointed out recently in an editorial by Gerbode.[1]

It is the purpose of this paper to illustrate the potentialities of such emergency treatment and the importance of the time factor in the outcome by brief presentation of a few cases.

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REPORT OF CASES

CASE 1.—A 70-year-old white man was admitted to the hospital on July 25, 1953, complaining of severe abdominal pain. He had been operated upon at another institution on March 14, 1953, at which time a large aneurysm of the abdominal aorta had been encountered. It was said to have measured 14×14×14 cm., to have originated 3.5 cm. distal to the renal arteries, and to have extended down to within 2.5 cm. of the aortic bifurcation. The aorta above and below the aneurysm was said to have been diffusely dilated. Because the patient was hypertensive and was thought to be a poor risk for a large surgical procedure, it was elected not to resect the aneurysm but to reinforce it with polyvinyl (Ivalon) sponge instead.

A few days before admission he had developed abdominal pain which became extremely severe on the day preceding admission. His physician noticed that the aneurysm was expanding and, on the day before admission, noted rapid enlargement of the abdominal mass. The patient looked acutely ill and was in excruciating pain. A very large mass was palpable in the abdomen, extending to the right of the midline and bulging into the left flank. The patient was in obvious circulatory collapse. The blood pressure was 100/60, and the pulse rate was 120. The red blood cell count was 2,370,000, and the hemoglobin, 6.2 gm. %. The circulation in both lower extremities was adequate, and both femoral and popliteal pulsations were palpable. The patient had not voided during the preceding 24 hours, and only 350 cc. of dilute urine was obtained when he was catheterized. It was obvious that the aneurysm had perforated and that the patient was in a near-terminal state. No homologous aortic grafts were available. Two grafts made of fused nylon and polyethylene were hastily constructed.* Because of the dilatation of the aorta said to have been present at the time of the first operation, they were made larger than the size of the usual aorta.

Shortly after admission, and a little more than 24 hours after the onset of severe pain, the patient was operated upon through a long midline incision.

* References 2 and 3.

The aneurysm had perforated, and bleeding had occurred throughout all the retroperitoneal tissues on the left side and into the abdominal wall. The aneurysm was much larger than that described at the time of the first operation. It began 1.5 cm. below the level of the renal arteries and extended into and included both common iliac arteries. It was possible to isolate the aorta above and the iliac arteries below with little or no loss of blood. No pulsation could be felt in the left external iliac artery. The vessels were occluded, and the anuerysm was excised. The proximal aorta was normal in size, and there was, therefore, a great discrepancy in size between the prepared grafts and the patient's aorta. The iliac extensions of one of the grafts approximated the size of the aorta proximally and the right common iliac artery distally. It was therefore interpolated between the aorta above and the right common iliac artery below. It was realized that the use of this graft would leave the patient without direct blood flow into the left common iliac artery. In view of the patient's desperate situation it was believed that this course of action would result in his best chance of survival, even though one extremity might be lost.

From the time of operation there was excellent pulsation in the right femoral and popliteal arteries, and the right lower extremity maintained good color and warmth. The left lower extremity, however, was totally ischemic up to the midthigh. The lower nephron nephrosis, present at the time of admission, continued. During the next 10 days the average urinary excretion was about 200 cc. a day, and the urine was poorly concentrated. During this time fluid intake was restricted and serum electrolytes were maintained at a near normal level. The serum potassium was kept within safe levels by the use of exchange resins and gastric suction. Eventually the patient died of uremia on the 10th postoperative day.

Postmortem examination revealed generalized arteriosclerosis, lower nephron nephrosis, moderate arteriolar nephrosclerosis, and passive congestion of the liver. The graft was patent and had a thin, smooth, glistening lining.

Case 2.—A 59-year-old white woman was admitted to the hospital on May 4, 1954, with excruciating abdominal pain. She had had a previous admission to the hospital in March, 1951. At that time she had a rather large abdominal aortic aneurysm. It was treated by wiring. Just after the small abdominal incision was closed, cardiac standstill developed. The chest was opened quickly; the heart was massaged, and resuscitation was accomplished. She had an uneventful convalescence and good health thereafter.

At about 9:00 p.m. on May 3, however, there was a sudden onset of excruciating abdominal pain. The pain radiated into the flanks and back and was constant. The patient vomited several times. Hypodermic injections of morphine brought about only partial relief of pain. She was transported about 65 miles by ambulance and was admitted to the hospital three and a half hours after the onset of pain.

She was complaining of excruciating pain in the abdomen and back. Her pulse rate was 92, and her blood pressure was 120/70. She was known to be moderately hypertensive. The extremities were cool, and she was sweating profusely. Her color, however, was relatively good. The hemoglobin was found to be 13.5 gm., and the red blood cell count, 4,290,000.

She was taken to the operating room less than six hours after the onset of pain. She had a very large aneurysm, which arose about 1.5 cm. below the renal artery and extended down to and included the first portion of both common iliac arteries. It had perforated posteriorly, and a moderate extravasation of blood in the retroperitoneal tissues had occurred. It was possible to isolate the aorta above and the iliac arteries below before entering the area of the hemorrhage. The aneurysm was excised, and a polyethylene-nylon graft was interpolated between the aorta above and the two common iliac arteries below. The patient tolerated the procedure well and had excellent pulsations in the arteries of her lower extremities at the completion of the operation.

She maintained good urinary output. She was discharged from the hospital on May 17.

When examined on Sept. 13 the patient stated that she was feeling very well and had been working steadily. She had excellent circulation in both lower extremities, and pulses in the abdominal aorta and in the femoral, popliteal, posterior tibial, and dorsal pedal arteries were normal. Her blood pressure was 160/80. She has remained well.

Case 3.—A 63-year-old white man was admitted to the hospital on Oct. 31, 1954, with excruciating abdominal, flank, and back pain of 16 hours' duration. He was in profound shock. The extremities were cold and wet. The blood pressure was 50/20; the pulse rate was 130, and the patient was very pale. There was a very large abdominal aneurysm.

He was taken immediately to the operating room, and a large aneurysm of the abdominal aorta was found. It had perforated posteriorly, and there was widespread extravasation of blood throughout the retroperitoneal tissues. It was possible to isolate the aorta above and the common iliac arteries below the aneurysm before getting into the area of extravasation. In addition, there was a large aneurysm of the right iliac artery. By the time the latter aneurysm was removed it was solidly thrombosed, and there was no retrograde flow of blood from the right external iliac artery.

It was, unfortunately, impossible to aspirate any thrombus from this vessel or to establish retrograde flow of blood. A nylon filter fabric graft [4] was interpolated between the aorta above and the left common iliac and right external iliac arteries below. The patient withstood the procedure well and was in relatively good condition at the completion of the operation.

He maintained excellent circulation in his left lower extremity. On the right side he had a good femoral pulse, but the right foot and the distal portion of the leg remained ischemic. The patient had not voided since the onset of pain the night before admission, and catheterization just prior to operation yielded only 200 cc. of urine of low specific gravity. He remained oliguric. Fluids were restricted, and every effort was made to keep his electrolytes at normal levels. It was necesary on two occasions to employ dialysis with an artificial kidney in order to combat dangerously high potassium levels. He died on Nov. 9, of uremia.

Postmortem examination revealed severe diffuse arteriosclerosis, lower nephron nephrosis, and arteriolar nephrosclerosis. The graft was patent and had a smooth lining.

CASE 4.—A 75-year-old woman was admitted to the hospital on Jan. 23, 1955, complaining of abdominal pain. On Jan. 12 she had suddenly developed very severe pain in her abdomen and back and had been admitted to a hospital in another community. Gradually the pain decreased in severity. It was the impression of her physician that she had had a small perforation of her aneurysm. On one occasion during her hospitalization she had developed an acute episode of auricular fibrillation. Digitalization was followed by conversion to a sinus rhythm.

At the time of admission she was relatively comfortable. There was some tenderness on palpation over the large abdominal aortic aneurysm. The circulation in both lower extremities was excellent. The blood pressure was 120/60, and the cardiac rhythm was regular. The hemoglobin was 10.5 gm. and the red blood cell count was 3,330,000. Serological tests for syphilis were negative. Electrocardiographic tracings showed nothing abnormal except digitalis effect. Radiograms revealed a tortuous ascending aorta and arch and calcification in the region of the abdominal aortic aneurysm.

She was operated upon on Jan. 26. She had a very large aneurysm, which extended from just below the renal arteries down to the bifurcation. Rupture had occurred, and there was extravasation in the retroperitoneal area. It was possible to to isolate the aorta above and the iliac arteries below before entering the region of the perforation. Before a graft could be interpolated, it was necessary to do a thromboendarterectomy of the distal end of the aortic bifurcation and both common iliac arteries. for they were so badly calcified and rigid that sutures could not be passed through the wall. A nylon filter fabric graft was interpolated in the aortic defect. There was excellent circulation in the right lower extremity at the completion of the operation but not in the left. Pulsation in the left external iliac artery was weak. This artery was opened, and no thrombus was found. The vessel was so badly diseased that it was necessary to do a thromboendarterectomy in order to close the incision. After the abdominal wound was repaired, the left femoral artery was exposed in the groin and just above the adductor tendon. Through small incisions in the artery it was possible to aspirate long segments of clot from the popliteal and tibial vessels. When the arteriotomy incisions were closed there was good circulation in the left foot.

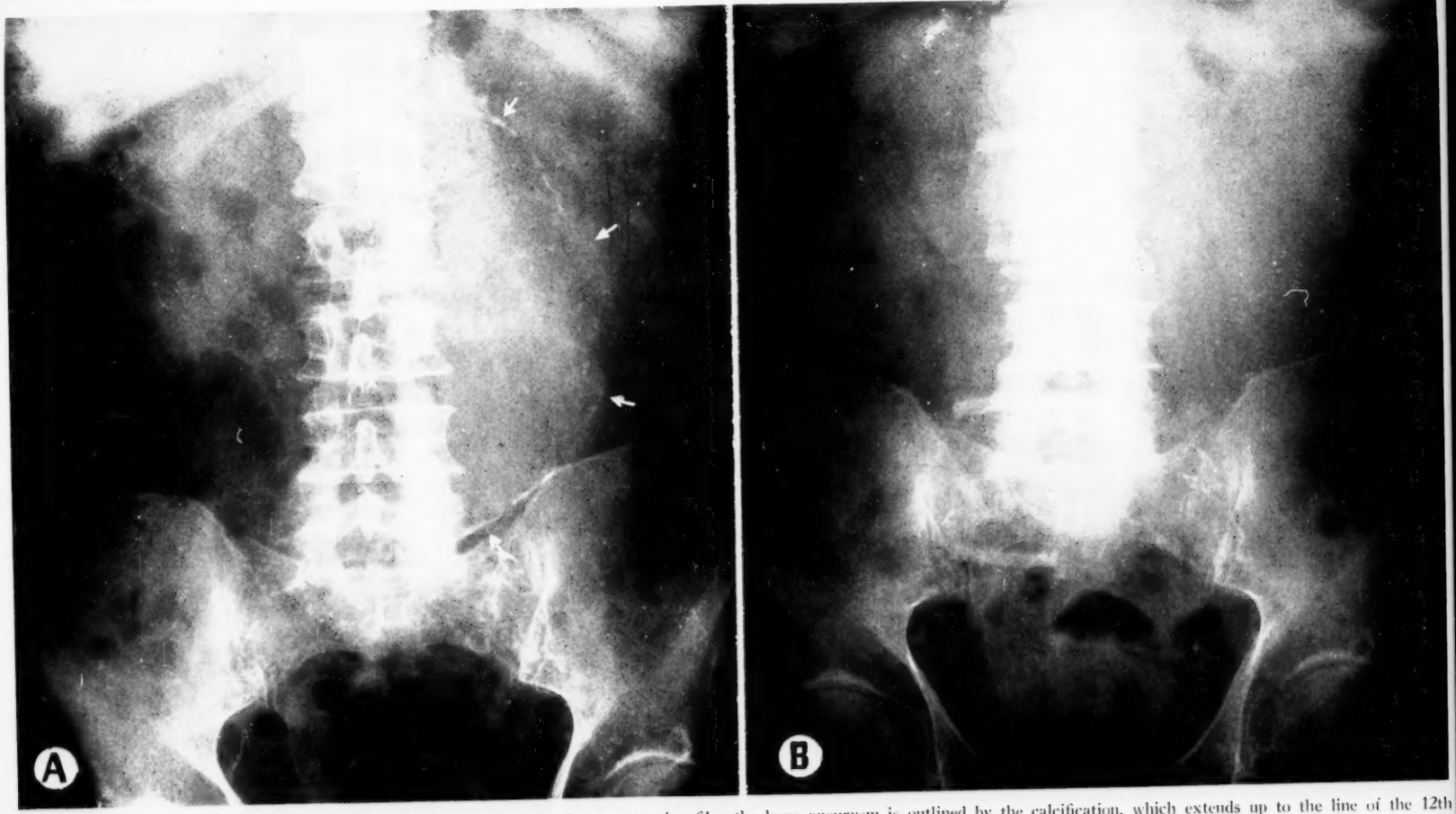
The patient had an uneventful convalescence. She maintained excellent circulation in both lower extremities and was discharged from the hospital on Feb. 5.

When seen on March 7, 1955, she had normal pulses in the abdominal aorta and in the femoral, popliteal, and dorsal pedal arteries. She has remained well.

CASE 5.—A 65-year-old man was admitted to the hospital on May 15, 1955. Two weeks previously, while working on the roof of a building, he fell and struck his back. He immediately developed severe lumbar back pain and pain in his left flank. The pain eased somewhat but persisted. On May 9 he had been admitted to another hospital, where a very large abdominal aneurysm was discovered.

He had had low back pain off and on for 20 years. In 1947 he developed an ulcer on the dorsum of the left foot and intermittent claudication in both calves. The ulcer healed. The claudication persisted and came on after walking one block. Both feet tended to be cold. He gave up tobacco in 1947. Tolazoline (Priscoline) was taken intermittently, with questionable improvement in the warmth of his feet and without effect upon exercise tolerance.

His blood pressure was 150/90. A huge pulsating mass was felt in the abdomen. It extended up beneath the costal margin. The femoral pulses were good. Popliteal pulses were not palpable, nor were dorsal pedal or posterior tibial pulses felt. The feet were cool and had poor venous filling. Oscillometric values were 2.5 in the right thigh, 0.5 in the left; 0.5 in the right calf, 0 in the left. The urine and blood examinations were essentially negative, and nonprotein nitrogen was 39 mg. per 100 cc. Roentgenograms revealed some cardiac enlargement, a tortuous descending thoracic aorta, a huge calcified abdominal aneurysm, and calcification of iliac and pelvic arteries. Electrocardiograms showed nonspecific ST-T changes over the left ventricle.



Roentgenograms in Case 5; *A*, preoperative; *B*, postoperative. In the preoperative film the huge aneurysm is outlined by the calcification, which extends up to the line of the 12th thoracic vertebra and might have been interpreted erroneously as indicating nonresectability.

He was operated upon May 17. Rupture of the aneurysm had been suspected, but there was no proof of its occurrence. The aneurysm was about 20 cm. long and 15 cm. in diameter. It arose immediately below the right renal artery and extended down to the bifurcation. Both iliac arteries were stony hard and dilated. There was a fair-sized old extravasation posteriorly and retroperitoneally to the left of the aneurysm. It was possible to gain control of the aorta above and the iliac arteries below and to free the right side of the aneurysm before entering the area of extravasation. The aneurysm had arisen so close to the renal arteries that the clamp across the aorta of necessity partially occluded the right renal artery. The entire abdominal aorta above the lesion was diffusely dilated. Its circumference was 18 cm. The iliacs were badly calcified. Thromboendarterectomy of the common iliac arteries was necessary before sutures could be passed through the aortic bifurcation stump. A straight nylon filter fabric graft, tailored to fit the aorta above and below, was constructed and sutured in place. The patient stood the procedure well.

His convalescence was uneventful, and excellent femoral pulses were maintained. The patient feels that his feet are warmer than they were in the past.

COMMENT

These cases illustrate some of the potentialities and limitations of the surgical treatment of perforated aortic aneurysms. In spite of rupture and extravasation of blood in the retroperitoneal tissues, it is usually possible, as it was in these cases, to isolate the aorta above and the iliac vessels below before entering the area of extravasation. It is thus ordinarily possible to restrict loss of blood to the same order of magnitude as in operations upon unperforated aortic aneurysms. As has recently been pointed out by Javid and his associates [5] and by Cooley and De Bakey,† it may be advisable in some cases first to occlude the distal thoracic aorta through a chest incision before proceeding to the abdominal dissection.

The operation is, however, more difficult when rupture has occurred. Furthermore, the period of aortic occlusion is apt to be considerably longer than in cases of unruptured aneurysms, for where rupture has occurred it is usually necessary to occlude the aorta proximally and the aorta or iliac arteries distal to the aneurysm before beginning any dissection of the aneurysm itself. In contrast, in elective operations upon aneurysms it is commonly possible to free the aneurysm in large measure before occluding the aortic pathway. As a consequence, there is probably an increased risk of thrombosis in the vessels of the extremity. Such thrombosis occurred in three of these five cases. In one (Case 4) it was possible to remove a large thrombus from the popliteal and tibial vessels and to restore perfect circulation to the involved extremity. Perhaps a femoral arteriotomy in Case 3 might have enabled us to remove the obstructing thrombus and prevent gangrene. Had a suitable graft been available in the first case, it is entirely possible that the obstructing thrombus could have been removed and circulation reestablished to the left lower extremity. This patient was the first in whom a plastic aortic graft was utilized, and, unfortunately, the grafts were made far too large because dilatation of the aorta above and below the aneurysm had been noted at his previous operation. In this case the iliac extension of one of the plastic grafts was deliberately interpolated between the aorta above and the right common iliac below, with full realization that ischemia would probably result in the left lower extremity. There was, however, no alternative. Subsequently, whenever a suitable graft has not been available, one has been constructed to measure during the course of the operation itself, as was done in Case 5. Though the risk of thrombosis is probably greater in cases of ruptured aneurysm, it is undoubtedly not as great as one would judge from our small experience.

Thrombosis in the distal arteries is, of course, a possible occurrence during elective surgery upon unruptured aortic aneurysms, and the injection of heparin into the distal arterial tree at the moment of occlusion of the aorta does not necessarily prevent distal thrombosis. We have, however, not had

† Cooley, D. A., and De Bakey, M. E., in discussion on Javid.[5]

gangrene develop following excision of any unruptured aneurysm, and only in two cases have we failed to reestablish perfectly normal circulation. In one of these exceptional cases a portion of the necrotic lining of the aneurysm passed down to the bifurcation of the femoral artery as an embolus. It was removed shortly after completion of the first operation, but, unfortunately, we were unsuccessful in maintaining a free flow of blood through the femoral artery. The patient, however, maintained excellent circulation and has no complaints. In the second exceptional case the iliac, femoral, and popliteal arteries on one side were almost totally occluded by a calcified thickened intimal lining. In this case it was necessary to do a thromboendarterectomy from the origin of the common iliac artery all the way down into the popliteal area. Though the femoral artery remained patent, there was some relative decrease in circulation in the affected leg and foot.

The importance of the time factor is obvious. In Case 2 the patient was transported to the hospital relatively soon and was operated upon approximately six hours after the onset of pain. Up to that time she h: lost compartively little blood and was in good general condition, though she had some hypotension and tachycardia. Her course was as uneventful as if the operation had been carried out as an elective procedure before rupture. In contrast, in the first and third cases the operation was performed after a long delay. In one, perforation had occurred approximately 16 hours beforehand; in the other some leak had undoubtedly occurred several days before and the perforation was clear-cut at least 24 hours before admission. In both these cases it was possible to extirpate the aneurysm and to interpolate a graft, but in neither case was it possible to restore kidney function. Both patients had been admitted to the hospital with a well-established lower nephron syndrome.

The fourth and fifth cases illustrate the fact that on occasion patients may have a relatively small leak from an aortic aneurysm perforation and survive for a period of time. The fact that this may occur does not, we believe, make it advisable to delay operative treatment in any case of suspected perforation. While the outcome was good in these particular instances, there is certainly every reason to believe that these patients would have withstood operative treatment just as well within a few hours after the onset of pain as they did some days later, and such treatment would have constituted an altogether safer course. Indeed, they should have been operated upon as soon as they came under our care, in order to forestall a second possible rupture. The policy of prompt operation seems mandatory, since there is no way of telling whether one is dealing with an exceptional instance of this sort, in which the patient may survive a small perforation, or whether one is dealing with the far commoner, larger perforations, which almost inevitably lead to death unless treated promptly. It is important that treatment be carried out with the least possible delay, not only because it gives the patient the greatest likelihood of surviving the procedure but also because it obviates the establishment of the lower nephron syndrome, which is almost certain to intervene if the patient remains in profound shock for any length of time.

In Case 1 it was obvious from the careful description of the operative findings at the first operation, made available to us, that the aneurysm had expanded very rapidly during the few months intervening between the two procedures. At the first operation the aneurysm began well below the renal arteries and ended proximal to the bifurcation. By the time perforation took place the aneurysm had extended upward almost to the level of the renal arteries and downward to involve the bifurcation. This potential steady increase in the size and extent of aneurysms is one reason why we should aim to detect aneurysms of the aorta early in the course of their development and to treat them when they are smaller, less ex-

tensive, and amendable to relatively easy surgical excision.

It is well established that remarkable palliation has not infrequently been achieved by some of the procedures which have been utilized in the past, such as internal wiring and the external application of membranes or solutions designed to produce fibrosis and strengthen the wall of the aneurysm. It is becoming equally clear, however, that these procedures offer little real protection against the threat of rupture. It is of interest in this connection that in two of the five cases reported such procedures had been carried out previously, polyvinyl sponge having been used in one and internal wiring in the other.

Though in the five cases reported it was possible to perform excision of the ruptured aneurysm and interpolation of a graft with safety, obviously surgical attempts to treat perforated aneurysms will result in an occasional operative fatality. Not long ago, as a last desperate resort, in another institution ‡ we undertook operation upon a patient who was pulseless and without obtainable blood pressure at the time the incision was made. This 61-year-old patient had long-standing arteriosclerotic heart disease with severe angina pectoris. He had had severe abdominal pain for 24 hours and had undergone profound circulatory collapse 7 hours before operation. During the hour preceding operation rapid administration of blood was associated with progressive deterioration, the pulse and blood pressure becoming unobtainable. Since no improvement was occurring with continued rapid administration of blood through two veins, it was obvious that his only chance lay in stopping the bleeding by surgical intervention, and it was equally apparent that the chance of success was small. Unfortunately, cardiac arrest occurred just as the situation was being brought under control by isolation and clamping of the proximal aorta. By this time he had received a total of 5000 cc. of blood. Certainly in this case the chance of a successful outcome would have been far greater had operation been undertaken earlier, before the onset of such profound circulatory collapse.

‡ Indianapolis Veterans Administration Hospital.

Recently an additional 29 cases have come to our attention.§ Of the 35 surgically treated cases, including our own, 14, or 40%, have died and 21, or 60%, have survived.

SUMMARY

It seems quite clear that aneurysms of the aorta should be treated when possible by excisional therapy in order to forestall the very serious consequences of these lesions. It is equally clear that when an aortic aneurysm ruptures every effort should be made to bring the patient to surgery without delay.

REFERENCES

1. Gerbode, F.: Ruptured Aortic Aneurysm—A Surgical Emergency, Surg., Gynec. & Obst. **98**:759, 1954.

2. Shumacker, H. B., Jr., and King, H.: The Use of Pliable Plastic Tubes as Aortic Substitutes in Man, Surg., Gynec. & Obst. **99**:287-294, 1954.

3. Shumacker, H. B., Jr.; Harris, E. J., and Siderys, H.: Pliable Plastic Tubes as Aortic Substitutes, Surgery **37**:80-93, 1955.

4. Harris, E. J.; Shumacker, H. B., Jr.; Siderys, H.; Moore, T. C., and Grice, P.: Experimental Comparison of Certain Pliable Plastic Materials as Aortic Grafts, A. M. A. Arch. Surg. **71**:449-459, 1955.

5. Javid, H.; Dye, W. S.; Grove, W. J., and Julian, O. C.: Resection of Ruptured Aneurysms of the Abdominal Aorta, Ann. Surg., to be published.

§ Javid[5] and Cooley, D. A., and De Bakey, M. E.; Gerbode, F.; Eiseman, B., in discussion of Javid.[5]

Experimental Closed Loop Obstruction of the Entire Colon

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The concept of the "closed loop" in acute intestinal obstruction is an important one. Clinically, this condition has been related to early fatal termination; experimentally, studies on closed loops have been made under varied conditions to better understand the precise mechanism of death in acute intestinal obstruction. These experiments and their relation clinically to complete obstruction have been concerned almost entirely with the small intestine.* Some of these observations have been applied to the colon by inference. However, there are no data available pertaining to the entire isolated colon closed at each end.

Bacteremia was only rarely found in fatal cases of acute intestinal obstruction by McKenna.[3] Hartwell and others,[4] after experimental studies on dogs, believed that death in intestinal obstruction was due to dehydration and to a toxin in the circulating blood. Murphy and Brooks [5] recovered toxic material from the thoracic ducts of animals which previously had such material injected into a distended intestinal loop. They concluded that death was due to a toxin formed as a result of bacterial growth and absorbed through damaged mucosa of the obstructed intestine. However, Carlson, Lynch, and Wangensteen [6] have transfused the entire blood content of toxic animals with various types of obstruction into normal animals without effect. Whipple and his associates,† Draper,‡ and others postulated that the toxemia of intestinal obstruction was due to perverted duodenal secretion or aberrant activity of duodenal or possibly pancreatic cells. Dragstedt's report [11] in 1918 disproved this. Draper [10] and Dragstedt and others § showed that isolated closed loops of the small intestine led to a rapidly fatal termination; the higher in the intestine that the loop was made the more rapid the fatality. Thus, duodenal closed loops produced a more spectacular picture of shock and so-called toxemia than ileal loops; short transverse colon loops were well tolerated for several weeks. Dragstedt further showed that the lethal factor depended largely on abnormal distention and the presence of bacteria in the bowel lumen. The mechanisms of dehydration were carefully studied by Gamble and Ross,[13] Elman and Hartman,[14] and Wangensteen and Leven [15] and were summarized by McIver.[16] This was a significant cause of mortality, especially in high obstructions. However, Elman found that parenteral administration of saline did not prolong survival in low ileal obstruction; he concluded that death was not due to electrolyte changes incident to dehydration and loss of gastrointestinal secretions, but rather to a profound circulatory failure or shock quite distinct from the circulatory impairment or dehydration from high obstruction.[14] Scott and Wangensteen [17] showed that the length of life after strangulating obstruction depended more on the type of strangulation produced than the length of the involved segment. In simple

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* References 1 and 2.

† References 7 and 8.

‡ References 9 and 10.

§ References 11 and 12.

obstruction gas accumulates in the proximal bowel in far greater amounts than within closed loop or strangulated segments.[18] Later, Wangensteen [19] summarized his experiments which stressed the importance of the mechanical effects of distention in obstruction of both small and large intestine. He held that these effects adequately account for mortality without invoking an unknown toxic factor. Estes and Holm [20] showed clinically and experimentally that obstructed ileal segments which were bypassed by shunting procedures remained dilated or went on to ulceration and perforation. More recently, it was demonstrated that the fatal outcome of closed small intestine loops with and without impaired circulation was prevented or delayed by the use of sulfa drugs || or antibiotics.¶

In the present problem we have attempted to test the behavior and survival of the isolated closed colon with intact circulation but divorced from ileal emptying. Under these circumstances, the study may be made of factors intrinsic in the colon itself which may contribute to morbidity and mortality in large bowel obstruction due to carcinoma of the colon. It would seem that the closed colon with its long stretch of lumen filled with material that could decompose, as well as heavy bacterial contamination, contains the important components necessary for a fatal result. However, we shall relate that the closed colon with ileal emptying excluded, is well tolerated and does not greatly distend. Apparently, the absorptive, secretory, and detoxifying processes adequately adjust to meet the situation.

MATERIALS AND METHODS

Mongrel dogs averaging 25 lb. and white rats averaging 300 gm. in body weight were used. The animals were in a fasting state for 12 to 29 hours prior to the operation. The dogs were anesthetized with intraperitoneal injections of veterinary pentobarbital (Nembutal) in doses of 15 mg. per pound of body weight. The rats were anesthetized in an ether box, and anesthesia was maintained with an ether cone. In all of the rats and most of the dogs the colon was excluded in a one-stage operation. The terminal ileum was divided close to the cecum, and the cecal end was then closed by Connel sutures of No. 00 chromic absorbable (gut) sutures reinforced with interrupted nonabsorbable surgical (silk) sutures. Distally, the colon was then divided below the rectosigmoid. No attempt was made to empty the colon of fecal material. The distal end was closed in a manner similar to the cecal end. An end-to-end ileoproctostomy was then done with a through-and-through suture of No. 00 chromic absorbable (gut) sutures and the entire circumference was reinforced with an interrupted seromuscular suture of fine silk. In the rat we used No. 0000 arterial silk for suturing. Some of the operations on dogs were done in two stages: ileoproctostomy was done first; two or three weeks later, the colon exclusion was done. None of the rats received any postoperative supportive therapy or antibiotics. About one-half of the dogs received the following supportive therapy: 500 cc. of 5% dextrose in saline parenterally, for three days; also penicillin G procaine (Crysticillin), 300,000 units daily for three days.

At postmortem examination special attention was paid to the condition and contents of the excluded colon loop. The serosa and mucosa were examined for viability, edema, and other pathological changes. The colon was weighed, the length of the segment was measured, and fluid, gaseous, and fecal volumes were determined. In some cases, bacteriologic study of colon content was done. In four dogs and three rats the gaseous content of the experimental loops was analyzed. The analyses were carried out in a modern gas analysis apparatus, with use of mercury as a confining liquid.[25] The apparatus has a 1000 ml. burette equipped with a compensator for temperature and pressure change, with bubbling absorption pipettes and a flushing manifold. Hydrogen sulfide was tested by means of a solution of cadmium acetate in 3% acetic acid; carbon dioxide, by 20% solution of potassium hydroxide; unsaturated hydrocarbons, by fuming sulfuric acid; oxygen, by alkaline pyrogallate solution; methane, by slow combustion in an atmosphere of oxygen, and nitrogen, by difference.

RESULTS

Six of twelve dogs operated on without supportive and antibiotic therapy died of anastomotic leaks. One of these deaths took place after the first stage. Four other animals died of incidental or intercurrent conditions—two of distemper, one of pneumonia, and one of an unrelated volvulus of the small

|| Reference 21 and Firor, W., and Poth, E., cited by Blain.[24]

¶ References 22 to 24.

intestine. The latter occurred on the 72nd postoperative day. The two remaining dogs were killed on the 68th and 88th days, respectively.

The ten dogs receiving supportive therapy and penicillin did much better. Only two died of anastomotic leaks, and one died of a volvulus of the closed colon loop on the 80th postoperative day. The seven remaining animals were killed at 14, 18, 71, 79, 102, 121, and 125 days postoperatively, respectively.

In four dogs no antibiotics were used preoperatively or postoperatively. However, because of the profuse and intractable diarrhea produced by ileoproctostomy, parenteral fluids were given during the first few days postoperatively. One of these animals died of an anastomotic leak, while the three other dogs remained well and healthy until their deaths 89, 448, and 453 days postoperatively, respectively.

Of 14 rats operated on, 6 died in the immediate postoperative period of anastomotic leaks or other technical errors. Two other rats died of abdominal wall infection 21 days postoperatively. The six remaining rats were killed at 7, 8, 21, 53, and 58 days, respectively.

Except for the one case of volvulus of the colon loop all colons in the four series were intact and healthy, with normal bowel wall and mucosa. Not one of the colons was greatly distended, although some contained more material than others. The large amount of fecal material retained in some of the dog colons was reduced to a soft homogeneous light brown pasty mass. Table 1 summarizes postmortem observations. Table 2 lists results of the gas analyses on four dog colons. The studies on the rat colons were spoiled by contamination with air; however, no hydrogen sulfide was present on qualitative testing. Bacteriologic studies on these colons as well as on the rat colons uniformly revealed colon-type bacteria and nonhemolytic anaerobic streptococci; occasionally Streptococcus fecalis was present.

TABLE 1.—*Average Measurements, Postmortem Closed Colon Loops*

15 Dogs (average wt., 25 lb.)	
Length of colon loop	24 cm.
Gas content	38 cc.
Liquid and solid content	89 cc.
10 Rats (average wt., 200 gm.)	
Length of colon loop	13 cm.
Gas content	1.4 cc.
Liquid and solid content	1.8 cc.

TABLE 2.—*Gas Analysis of Experimental Closed Colons*

	Dog No.			
	13	16	18	19
Gas recovered, cc.	41	51	30	24
Hydrogen sulfide, %	0.0	0.0	0.0	0.0
Carbon dioxide, %	6.3	6.0	8.8	8.8
Unsaturated hydrocarbons, %	0.0	0.0	0.0	0.0
Methane, %	10.1	8.6	6.2	6.2
Nitrogen, %	83.6	85.4	85.0	85.0

COMMENT

Physiologically and bacteriologically, the large and small intestines differ; so, it might be expected that the colon would behave differently as a long closed loop. Clinically and pathologically the two entities present further differences. The mechanisms producing small bowel obstructions (adhesive bands, hernias, volvulus, intussusception, and extrinsic lesions) not only produce obstruction but immediately initiate circulatory embarrassment in the mesentery and the bowel wall itself. By contrast, large bowel obstruction is most frequently caused by carcinoma of the colon. After variable periods of partial obstruction the site of the colon lesion may suddenly become completely occluded as a result of an acute inflammatory process, necrosis, or obturation.[26] At the proximal end, the ileocecal sphincter and valve mechanism tend to prevent reflux from the closed loop.[27] The ileum, up to some limit, continues to empty into the colon. We have found it convenient to refer to this type of clinically obstructed colon as a "tension closed loop." It will be noted that the general circulation of the colon wall remains intact until rather late in the course of the process, when it becomes gradually and insidiously embarrassed by rising hydrostatic pressure in the large intestinal lumen.

The experimentally closed colon with ileal emptying excluded not only survived for long periods, but was grossly and histologically healthy in the killed animal. To a large extent the liquid and gaseous materials were absorbed. This was also true of the group of animals who received no antibiotic therapy before or after the exclusion operation.

As late as 1934, McIver,[16] in his monograph, stressed the importance of decomposition of intestinal content in the production of distention in bowel obstruction. This applied particularly to the colon, wherein the huge distention seen clinically was ascribed to fermentative production of gases. Even today some still hold to this theory. In 1935 Wangensteen,[28] in his Samuel D. Gross prize essay, summarized the experimental evidence which indicated the true origin of the distending gases. He pointed out that about 68% was swallowed air. Of the remaining 32%, 70% entered the bowel lumen by diffusion from the blood, and 30% was formed by decomposition of the material in the bowel lumen. Our experiments suggest that the liquid and gaseous material in distended large bowel comes largely from ileal emptying into the cecum and not from decomposition of fecal material. If ileal emptying is excluded, animals are able to tolerate closed loop obstruction of the colon indefinitely. The colon does not go on to rupture. Noxious gases and products of putrefaction if formed are absorbed and detoxified; bacteria within the closed loop are tolerated, and chemical and enzymatic products are not an obvious problem; mucus continues to be produced but in diminished quantities, and the liquid content of the feces is gradually absorbed.

In patients with large bowel obstruction absolute prohibition of oral intake and Wangensteen type gastric suction assume some importance as therapeutic measures. While we cannot decompress the colon directly with Levin tube or even long tube suction, such suction and nothing by mouth will prevent or minimize associated small intestinal distension[26] and the effect of small intestinal emptying into the colon.

SUMMARY

Experimental closed loops of the entire colon were made in 26 dogs and 14 rats with and without antibiotic and supportive therapy.

In each group the mortality was not determined by the closed colon loop. Without exception, penicillin or not, this loop survived and at death was found to be intact and distended moderately or not at all.

Gross, histologic, bacteriologic, and gas analysis studies are reported.

The clinical significance of these results in relation to acute closed colon loop obstruction is indicated.

REFERENCES

1. Stone, H. B.; Berheim, B. M., and Whipple, G. H.: Intestinal Obstruction, Bull. Johns Hopkins Hosp. **23**:159, 1912.

2. Hartwell, J. A., and Hoguet, J. P.: An Experimental Study of High Intestinal Obstruction, Am. J. M. Sc. **143**:357, 1912.

3. McKenna, C. H.: Drainage of the Upper Intestinal Loop for the Relief of Ileus, Surg., Gynec. & Obst. **17**:674, 1913.

4. Hartwell, J. A. Hoguet, J. P., and Beekman, F.: An Experimental Study of Intestinal Obstruction, Arch. Int. Med. **13**:701, 1914.

5. Murphy, F. T., and Brooks, B.: Intestinal Obstruction, Arch. Int. Med. **15**:392, 1915.

6. Carlson, H. A.; Lynch, F. W., and Wangensteen, O. H.: Transfusion of Portal Blood from Dogs with Obstruction to Normal Recipients, Proc. Soc. Exper. Biol. & Med. **28**:542, 1931.

7. Whipple, G. H.; Stone, H. B., and Berheim, B. M.: Intestinal Obstruction: A Study of a Toxic Substance Produced in Closed Duodenal Loops, J. Exper. Med. **17**:286, 1913.

8. Stone, H. B.; Berheim, B. M., and Whipple, G. H.: The Experimental Study of Intestinal Obstruction, Am. J. Surg. **59**:712, 1914.

9. Draper, J. W.: Experimental Intestinal Obstruction, J. A. M. A. **57**:1338, 1911.

10. Draper, J. W.: Intestinal Obstruction, J. A. M. A. **67**:1080, 1916.

11. Dragstedt, L. R.; Moorhead, J. J., and Burcky, F. W.: Intestinal Obstruction, J. Exper. Med. **25**:421, 1917.

12. Dragstedt, L. R.; Dragstedt, C. H.; McClintock, J. T., and Chase, C. S.: A Study of the Factors Involved in the Production and Absorption of Toxic Materials from the Intestine, J. Exper. Med. **30**:109, 1919.

13. Gamble, J. C., and Ross, S. G.: The Factors in the Dehydration Following Pyloric Obstruction, J. Clin. Invest. **1**:403, 1925.

14. Elman, R., and Hartman, F.: Experimental Occlusion of the Terminal Duodenum and Ileum, Surg., Gynec. & Obst. **53**:307, 1931.

15. Wangensteen, O. H., and Leven, N. L.: Correlation of Function with Cause of Death Following Experimental Intestinal Obstruction at Varying Levels, Arch. Surg. **22**:658, 1931.

16. McIver, M. A.: Acute Intestinal Obstruction, New York, Paul B. Hoeber, Inc., 1934, p. 178.

17. Scott, H. G., and Wangensteen, O. H.: Length of Life Following Various Types of Strangulation Obstruction in Dogs, Proc. Soc. Exper. Biol. & Med. **29**:424, 1932.

18. Scott, H. G.; Dvorak, H. J.; Borman, C. N., and Wangensteen, O. H.: Comparative Study of the Quantity of Gas in the Bowel in Simple and Closed Loop Obstruction, Proc. Soc. Exper. Biol. & Med. **28**:902, 1931.

19. Wangensteen, O. H.: Intestinal Obstruction, Ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1942, p. 38.

20. Estes, W. L., and Holm, C. E.: The Fate of the Obstructed Loop in Intestinal Obstruction Following an Anastomosis Around the Obstruction, Ann. Surg. **96**:924, 1932.

21. Sarnoff, S. J., and Fine, J.: Effect of Chemotherapy on the Ileum Subjected to Vascular Injury, Ann. Surg. **121**:74, 1945.

22. Harper, W. H., and Blain, A., III.: The Effect of Penicillin in Experimental Intestinal Obstruction, Bull. Johns Hopkins Hosp. **76**:221, 1945.

23. Farris, J. M., and Romack, H. H.: Effect of Streptomycin in Closed Loop Appendicitis, Surgery **22**:305, 1947.

24. Blain, A., III.: Penicillin in Experimental Intestinal Obstruction, Surg., Gynec. & Obst. **84**:753, 1947.

25. Ulin, A. W.; Grotzinger, P. J., and Cattie, V. J.: Experimental Studies on Closed Colon Loops, S. Forum, (1951) pp. 105-111, 1952.

26. Ulin, A. W.; Grotzinger, P. J.; Sacks, C. L., and Martin, W. L.: Diagnostic and Therapeutic Problems in Large Bowel Obstruction Due to Carcinoma of the Colon, Pennsylvania M. J. **53**:1290, 1950.

27. Ulin, A. W., and Deutsch, J.: Visualization of Ileocecal Papilla in a Living Subject, Gastroenterology **16**:444, 1950.

28. Wangensteen, O. H.: The Therapeutic Problem in Bowel Obstruction, Springfield, Ill., Charles C Thomas, Publisher, 1937, Pt. 1.

Submucous Lipoma of the Transverse Colon

Report of a Case

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Submucous lipoma is the second commonest benign neoplasm of the gastrointestinal tract. However, its appearance not infrequently causes surprise, and its true nature may not be suspected until after an extensive surgical procedure has been carried out to remove it. The lesion is thus very important because it occurs in patients of the cancer age. In dealing with these persons, the surgeon is conditioned to removing lesions with adjacent normal tissue. The recognition of the true nature of the lesion is most important, if it be a submucous lipoma. Fortunately, this lesion can be easily identified at surgery, in most instances, if it is suspected. With this in mind, an illustrative case of lipoma of the colon is reported which showed all the characteristics of such a lesion. This report and attendant discussion may serve as a reminder of the existence of such a surgically pleasant lesion.

REPORT OF CASE

A 79-year-old white farmer was admitted to the Seattle Veterans Administration Hospital on Feb. 8, 1954, with a history of increasing gastrointestinal distress over an 8- to 12-month period. The patient had been constipated chronically for 30 to 40 years, but this particular difficulty had been easily managed with the use of proprietary cathartics. During the eight months prior to admission, however, constipation had become so severe as to require medication producing a liquid stool for relief. Anorexia had also been a prominent feature during this 8- to 12-month period, and the patient alleged that he had lost 36 lb. in weight (a decrease from 180 lb. to 144 lb.) and much strength during this time. During the two to three months immediately preceding admission, he had experienced gripping pain in both lower quadrants of increasingly severe intensity, occurring three to four hours after meals. The patient had been treated symptomatically during the previous year for angina pectoris and for prostatic hyperplasia.

Physical Examination.—Temperature, 98.6 F; pulse rate, 80; respiratory rate, 18; blood pressure, 106/70. The patient was a well-developed, poorly nourished, deaf white man with evidence of recent weight loss. The skin was pale and dry, with poor turgor. The heart had a regular rhythm and was not enlarged, but a Grade 2 apical systolic murmur was present. The lungs revealed only a few fine basilar rales. Moderate tenderness was present on deep palpation of the left flank in the region of a palpable spleen. Moderate tenderness was also present on deep palpation of the right upper quadrant, but no definite mass was felt. The prostate was uniformly enlarged to about three times normal size.

Laboratory Data.—Urine was essentially normal. Hemoglobin was 14.8 gm. per 100 cc.; hematocrit reading was 44%, and the cell indices were normal. White cell count was 10,600, with 68% polymorphonuclear leucocytes and 26% lymphocytes. ESR was 4 mm/hr.; BSP was 3% in 45 minutes; BUN was 12 mg. per 100 cc. Kahn test was negative.

Course in the Hospital.—Preliminary laboratory work revealed positive tests (guaiac) for occult blood in the stool repeatedly (five times). Venous pressure was normal (140 mm. of water), but the circulation time was slightly prolonged (20 seconds, dehydrocholic acid [Decholin], arm-to-tongue), and the ECG showed a definitely abnormal tracing. Sigmoidoscopy, on Feb. 12, was negative to 20 cm. Chest x-ray, on Feb. 10, showed some calcification of the aortic arch but normal configuration of the heart and the great vessels. The lung fields were clear. Barium enema, on Feb. 10, was inconclusive. Upper gastrointestinal series, on Feb. 15, showed no lesion. A repeat lower bowel study, on Feb. 18, revealed a "well-circumscribed, space-occupying" intrinsic mass in the region of the hepatic flexure, beyond which barium would not flow (Fig. 1).

The clincal impression was that the patient had arteriosclerotic heart disease, compensated, with

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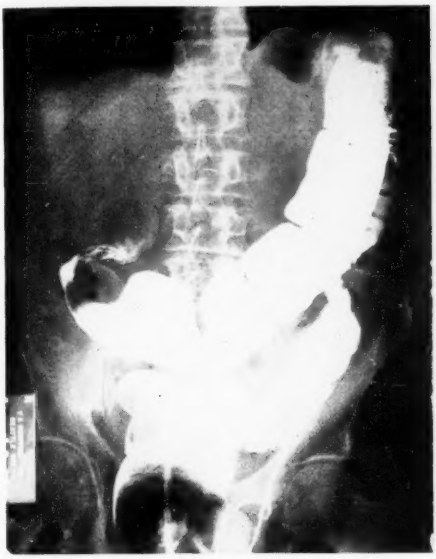


Fig. 1.—The x-ray picture of the barium enema in this patient showed a large, smooth, rounded obstructing filling defect in the hepatic flexure of the colon. This lesion was quite justifiably called a carcinoma by the radiologist, although the smooth outlines of the mass were noted as being unusual.

angina; benign prostatic hyperplasia, and some, possibly malignant, lesion of the colon.

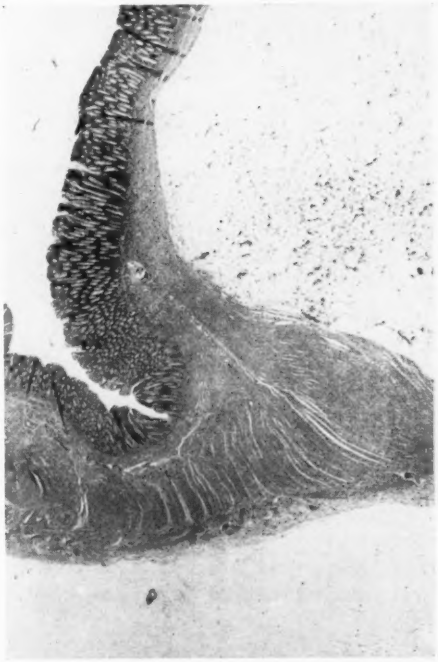
After digitalization and observation, the patient was prepared for surgery with vitamin K and succinylsulfathiazole (Sulfasuxidine). On March 9, exploration of the abdominal cavity was entirely negative except for a mass 6 cm. in diameter in the transverse colon near the hepatic flexure. This portion of the colon and mesocolon was removed by wedge resection. The postoperative course was uncomplicated. The patient went home on the ninth day. He has remained well since (one year).

The tumor removed was a 5×3.5 cm. oval, discrete, submucous mass. There was no ulceration.

Fig. 2.—Resected hepatic flexure of the colon shows a strange, soft, bosselated epithelialized mass protruding into the lumen of the rectum. It had a greenish-yellow hue when examined closely.

Fig. 3.—The lesion shown in Figure 2 was cut open through its intraluminal surface. The mass has the diagrammatic contour and consistency of a lipoma.

Fig. 4.—Low-power photomicrograph of the border of the lipoma depicted in the preceding illustrations shows the submucous location and distinct outlines.



The lesion was completely encapsulated and consisted of firm, yellow fat. This fat, when seen through the mucosa, was a greenish-yellow (Fig. 2, 3, and 4).

COMMENT

Comfort,[1] in 1931, summarized 181 cases of submucous lipoma of the gastrointestinal tract; 22 were in the stomach, 65 in the small bowel, and 92 in the large intestine or rectum. Pemberton and McCormack,[2] in 1937, summarized 116 cases confined to the large bowel. Gault and Kaplan,[3] in 1941, abstracted 13 more cases from the literature and reported a personal case. In 1950, Cavanaugh [4] reported 1 case and summarized 21 more from the literature, bringing the total of cases involving the colon to 152 at that time.

In the series of Pemberton and McCormack, those patients with symptoms whose age was known averaged 47.5 years, the range being 16 to 83 years of age. Those without symptoms averaged 63 years of age, the range being 35 to 83 years. In Cavanaugh's series, the average age was 52, the patients ranging from 25 to 75 years. Women predominate in the reported series. This is in contrast to the generally held 2:1 male-to-female ratio for large bowel cancer. The diagnosis of this lesion cannot be made preoperatively unless the lesion can be visualized for biopsy per anum. The diagnosis can be suspected radiographically.[2] The peculiar greenish color of the denuded mucosa overlying the tumor seen *in situ* is said to be highly suggestive of fat, but in most cases the diagnosis will still be made only after the lesion has been removed surgically.

The duration of symptoms varies, but in one series of 63 symptomatic patients the average was 41.5 months.[2] In another series, the patients had complaints for 2 days to 20 years.[3]

On grouping the frequency of the various symptoms in the reported series to date, one finds that pain, usually colicky, sharp, and brief, was present in 90 patients and was thus the most frequent complaint. Constipation followed, being present in 67 patients. Blood in the stool is not considered a reliable sign because of the variability in observation by the patient, but was reported to be present either on inspection or by chemical test in 40 patients. Weight loss was present in 23 patients, probably being due to the avoidance of colic-producing foods. Other symptoms, in order, were diarrhea (15 patients), anemia (8), nausea (7), "gas" (7), vomiting (5), tenesmus (3), anorexia (2), chills (1), alternating constipation and diarrhea (1).

Pemberton and McCormack divided the patients into two classes. The patients with prolonged histories, including gradually increasing constipation, recurring attacks of abdominal pain, and often nausea and vomiting after the intake of heavy and bulky foods, may suffer intermittently for many years. Their attacks may last for several days and terminate with bloody diarrheal stools. The differentiation from carcinoma is difficult. Other patients have the symptoms of acute bowel obstruction and may even have right lower quadrant pain, depending upon the location of the lesion. Here the differential diagnosis of appendicitis and diverticulitis must be considered.

Location of Reported Lipomas of the Colon

Location	No. of Cases	Percentage
Ileocecal valve	1	....
Cecum	35	....
Ascending colon	25	....
Hepatic flexure	1	45.2
	62	
Transverse colon	26	19.0
Splenic flexure	4	....
Descending colon	13	....
Sigmoid colon	18	25.6
	35	
Rectum	14	10.2
Multiple	1	....
Colon	10	....
Probable colon	2	....
Possible colon	2	....
	15	
Total number	152	

The location of the reported lesions is listed in the Table. The ascending colon seems to be the commonest location, with the sigmoid next in frequency.

Several types of pathological change may take place in these lesions. Most of the symptomatic lesions produce symptoms because of their growth to a size that causes obstruction of varying and increasing degree. About one-third of submucous lipomas produce symptoms because of intussusception, the tumor being drawn along by peristalsis ahead of trailing bowel. The number of tumors in which erosion of the mucous membrane covering the dome of the tumor produces a slow hemorrhage is difficult to determine from the literature, but this process probably occurs to some degree in all lesions of symptomatic size. Strangulation of a lipoma has not been reported, perhaps because of the usually broad pedicle, but it is theoretically possible.

A variety of procedures have been performed for treatment of these lesions, ranging all the way from cautery removal to right hemicolectomy and abdominoperineal resection. In one reported series, one lesion was "shelled out"; one was "excised," and one was removed by cautery. In another series of 25, three lesions were locally excised without resection. A higher percentage of local treatment is probably not consistent with good surgical technique, inasmuch as the suspicion of carcinoma usually is overwhelming and anything less than block excision for localized operable carcinoma is reprehensible.

The most important factor in proper treatment of submucous lipomas seems to be an awareness of the existence of such a lesion. If there is any doubt regarding the diagnosis, the lesion should be treated as carcinoma. Fortunately, if the diagnosis is suspected, the differentiation from malignant growth is usually easily made, and wide excision is thereby avoided.

CONCLUSION

A case of submucous lipoma of the transverse colon is presented. This lesion is rare and will probably continue to be diagnosed preoperatively as carcinoma. Treatment need be only simple local removal, but because of the preoperative diagnosis segmental resection probably will predominate.

REFERENCES

1. Comfort, M. W.: Submucous Lipomata of the Gastro-Intestinal Tract, Surg., Gynec. & Obst. **52**:101-118, 1931.

2. Pemberton, J. de J., and McCormack, C. J.: Submucous Lipomas of the Colon and Rectum, Am. J. Surg. **37**:205-218, 1937.

3. Gault, J. T., and Kaplan, P.: Submucous Lipoma of the Colon: Report of a Case, Am. J. Surg. **53**:145-151, 1941.

4. Cavanaugh, H. N.: Submucous Lipoma of the Large Bowel: Case Report with Review of the Literature, Am. J. Surg. **80**:860-864, 1950.

Cathode Ray Sterilization of Bone Grafts

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The purpose of this report is to record the results of experiments in the use as grafts of homogenous bone which was irradiated by high-voltage cathode rays. Development of practical methods for the storage, without significant deterioration, of tissues for clinical use as grafts has created a demand for tissue banks, and with the establishment of these banks new procedures for sterilization and preservation are constantly being investigated. With respect to bone there are advantages and disadvantages to each of the several techniques now in use. Currently the most popular method is that of storage at — 20 to — 30 C of bone, obtained under sterile conditions, from amputations, thoracotomies, or other surgical operations. The uncertainty of occurrence of these sources of supply has led to a search for alternative methods. The use of autopsy bone, being much more easily available and offering ideal selection of specimens, presents the difficulty of sterilization without that degree of denaturation of the proteins which would render the tissue reaction to the graft unfavorable. In this regard the adaptation to the problem of the method of sterilization by high-energy cathode-ray irradiation, originally developed for preservation of foods [1] and used successfully at the Children's Medical Center, Boston, by Meeker and Gross for aortic grafts,[2] suggested itself.

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MATERIALS AND METHODS

The plan of the experiment was to compare the histology of the tissue reactions with inlay grafts of homogenous, refrigerated unirradiated bone and homogenous, refrigerated irradiated bone. The experimental animals were adult cats, which were healthy and active. They were housed in small groups in wire mesh cages. One cat served as the donor for all the others. It was killed and each of the major long bones was dissected free of soft tissue and marrow; the cortical portions were then divided into many small segments, each measuring 10×4×3 mm. The number of segments was sufficient to satisfy the bacteriological and surgical portions of the experiment, so that all of the grafts were handled under the same conditions. About half of the grafts, in addition to contamination by handling, were dipped in broth cultures of Escherichia coli, Staphylococcus aureus, or Bacillus prodigiosus before packaging. Each specimen was then sealed separately in double polyethylene bags * and stored at — 20 C until the time of irradiation. At that time the specimens were transported in the frozen state to the Van de Graaff accelerator at the Massachusetts Institute of Technology, where half their number were exposed to 2,000,000 rep of cathode-ray irradiation, under the supervision of Mr. Kenneth A. Wright.† During exposure and transport the specimens were kept frozen by contact with carbon di-

* Obtained as tubing from Chippewa Plastics Co., Chippewa Falls, Wis.

† The irradiation procedure was administered through the courtesy of Prof. John G. Trump, Massachusetts Institute of Technology Department of Electrical Engineering, aided by a grant from the National Institutes of Health, for Sterilization of Blood Plasma and Fractions with High Energy Electrons.

oxide snow. Thereafter, the specimens were stored at —20C until used.

Twenty specimens were taken at random for bacteriological culture. Selection included irradiated and nonirradiated specimens which had been dipped in each of the broth cultures as well as those undipped. These specimens were ground in a mortar and cultured in thioglycollate broth and blood agar. In addition, five specimens of human cortical bone, obtained at autopsy and measuring maximally 2 cm. in thickness, were dipped, packaged, irradiated, and cultured in a manner identical with the experimental material except that all sides of these specimens were scraped to provide the inoculum.

For the grafting procedures 24 cats were used. The femur and tibia of each cat were the recipient sites, and each bone underwent the following surgical procedure. With the animal under intraperitoneal pentobarbital (Nembutal) anesthesia and with aseptic precautions, the shaft of the bone was exposed in its midportion. After the periosteum was elevated, a slot 4 mm. in width and 2 cm. long was cut into the marrow cavity with a rotary electric saw. Into this slot two graft specimens were inlaid,[3] the proximal one having been irradiated and the distal one unirradiated. The graft specimens, as described above, were allowed to thaw just prior to insertion and were pared down as necessary to fit the recipient slot exactly. The grafts were placed so that their outer surface was flush with that of the adjacent bony cortex, and no sutures were used except for skin closure. In each animal one caudal extremity (femur and tibia) was grafted at a sitting, and the identical procedure was performed on the other extremity after two, four, or six weeks, according to a schedule which arranged the dates of killing to yield equal numbers of specimens in each healing stage.

The stages of healing selected were 2, 4, 6, 8, 12, and 16 weeks postoperatively. Sixteen specimens represented the material for each healing stage. All of the cats tolerated the procedure well and showed no postoperative disability, infection, or fracture.

Killing of the animals was by overdosage of pentobarbital given intraperitoneally. The midportion of each bone operated on was excised with periosteum intact. After its proximal portion was marked with India ink, it was fixed in 10% formalin and decalcified in 5% nitric acid. Two blocks were cut from each specimen representing cross sections through each of the grafts, the proximal one being marked with India ink. The blocks were then imbedded in celloidin, sectioned, and stained by iron hematoxylin and eosin. The sections were so mounted on slides that each slide contained a section of the irradiated graft on the left and the nonirradiated control from the same bone on the right with the grafted areas approximated for easy microscopic comparison.

RESULTS

The bacteriological cultures of all of the irradiated specimens showed no growth. Organisms were recovered from all of the nonirradiated specimens with the exception of one specimen which had not been dipped in any of the bacterial cultures.

The results of the histological comparison may be summarized as follows. There was no detectable difference in the reaction at the recipient site to the two types of grafts during any of the stages of healing studied. Detailed descriptions of histological features of each group of specimens will therefore be omitted.

The histological appearance of the grafts in all of the sections in which they appeared was that of devitalized bone, manifested by lacunae free of osteocytes, and evidence of gradual resorption of the substance of the grafts on all available surfaces. The staining reaction of the grafts was the same as that of the surrounding living bone. In general a part of the grafts survived for the entire period of the experiment, but in a few instances the 16-week specimens showed full resorption of both the irradiated and the nonirradiated grafts. As the period of repair lengthened, the remnants of the graft decreased in size, but there was no difference in the rate of disappearance of irradiated and nonirradiated grafts.

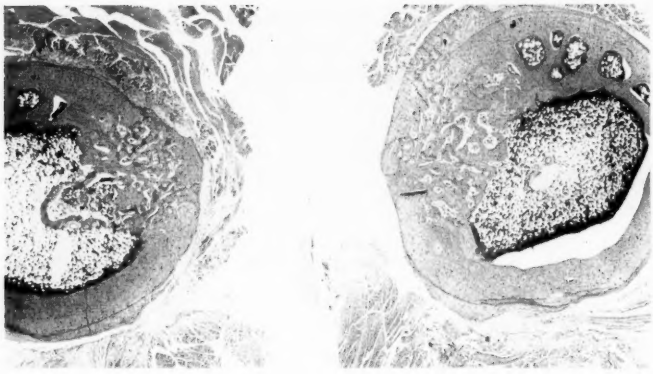

Fig. 1.—Implants six weeks postoperatively. On the left the irradiated specimen shows a small segment of graft remaining, approximately half of the width of the slot. It is confluent with the callus. Several areas show resorption.

The only reaction at the recipient site seen initially was hemorrhage with minimal inflammatory reaction to it. In many of the sections there persisted a line of devitalized bone at the border of the slot (Fig. 1) which took a deep blue stain and which remained free of callus, while the adjoining bone showed the normal accumulation of callus on its surface. This devitalization of the border of the slot was attributed to the heating caused by the saw. The specimens representing two weeks of repair showed very little callus in the majority of specimens, but after four weeks there was profuse accumulation of callus, sometimes sufficient to fill the entire marrow cavity. In no instance was there unequivocal evidence that the graft, whether irradiated or unirradiated, contributed in the formation of the callus.

The maximal production of callus was seen in the four-week specimens. It usually enveloped the grafts on all sides and was confluent with them; the absence of osteocytes in the graft's lacunae and the accentuation of the irregular cement line at the border of each graft allowed accurate delineation of its extent. The subsequent healing periods were characterized by increasing maturity of the callus and diminution in its extent, so that at 12 weeks (Fig. 2) the cortex was nearly reconstituted and at 16 weeks, in the few specimens where the grafts had completely disappeared, the graft area could be distinguished only by the patterns of cement lines and of Haversian canals.

There was much variation in the specimens from any single healing stage. Frequently the irradiated graft would show more marked absorption than its irradiated control or the surrounding recipient bed would show more advanced repair, but just as frequently the reverse was true. Therefore the figures have

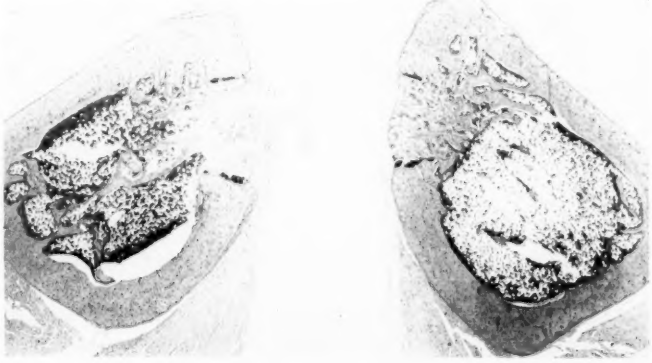

Fig. 2.—Implants 12 weeks postoperatively. The irradiated specimen on the left shows the effects of burning by the saw, but the callus has filled the gap and only a very small remnant of graft is present. The unirradiated graft on the right shows nearly an identical picture.

been selected to illustrate single instances in which the reactions were similar in order to portray the summation of the histological features of the two groups.

In a few instances technical errors provided interesting control material for histological study. When a graft did not maintain its original implantation site, usually because of postoperative hemorrhage which floated it out of its inlaid position, the reactions of the recipient bed were of interest. The production of callus in these instances was prompt and profuse; not enough material was available, however, to decide whether quantitatively it exceeded or fell short of that of specimens in which the grafts maintained their position. It seemed evident however that in respect to the graft itself, when displaced, its absorption was more rapid.

COMMENT

The ability of cathode rays (electrons) to kill bacteria was demonstrated as early as 1919.[4] Wide application of this sterilization technique became possible when there was devised an instrument which would produce a beam of electrons of sufficiently high voltage so that adequate penetration and short exposure time were possible. The Van de Graaff electrostatic generator [5] was the first such instrument, and the characteristics of its radiation have been well described by Trump, Wright, and Clarke.[6] Since the fundamental characteristics of high-energy cathode-ray irradiation are unfamiliar to most physicians and since they differ so much from the more familiar roentgen irradiation, the following data are presented to clarify several of the details of procedure. For additional information the reader is referred to the above-cited works and to a recent review of the subject.[7]

The beam of electrons produced by the Van de Graaff accelerator can penetrate any medium in proportion to its density and to the voltage of the beam. During their passage the electrons cause ionization, which in turn is responsible for the biological effects on bacteria and on tissue. The amount of ionization which is caused by the electron beam describes a characteristic curve, as shown by Trump and others, from which the dosage is calculated. Since all portions of the specimen must receive the safe bactericidal dose, which has been estimated at 1,500,000 rep, certain limits on the thickness of specimens and their packaging must be defined.

The density of glass limits its use as a packaging material, since the penetration of the cathode ray is thereby reduced. The polyethylene bags, primarily used because of their low density, have proved better than glass containers, since they take up less space in the deep freeze and show less frost, thus allowing the exact character of the enclosed specimen to be more easily ascertained. Incidentally it has been found that tubing 0.006 in. in thickness is necessary to provide adequate mechanical protection and transparency while minimizing evaporation.

The thickness of the specimen to be irradiated at 3,000,000 volts is also limited by the penetration of the electrons, and for bone, theoretically, the thickest specimen one can irradiate under these conditions is about 1.4 cm. This figure is arrived at from the following data. The maximal density (specific gravity) of cortical bone is given as 1.9, although we have found the specific gravity to vary from 1.35 for whole bone (dog, cat, and human) to 1.85 for clean cortical bone without marrow. Since the penetration of the electron beam is proportional to the density of the absorber and the maximal penetration in water is 1.7 cm., maximal penetration of bone will be 1/1.9 of 1.7 cm., or about 0.8 cm. While this maximal penetration is calculated for maximal density of the bone throughout its thickness, the latter never exists as such, since areas of less density such as Haversian canals or cancellous interstices occur in all bone. Nevertheless, for theoretical safety a depth of 0.7 cm. $\times$ 2 has been calculated for cortical bone, when irradiation is administered from two opposite surfaces at the same dosage. This theoretical limit may be lower than that actually possible in practice as our human bacteriological controls indicate, and if greater depth of penetration is needed, equipment with higher voltage may be used.

The bacteriological studies of Meeker and Gross [2] and others,[7] confirmed in the present report, indicate that this theoretical limit is safe in practice. While samples of cortical bone, even from human adult femur, will rarely reach 1.4 cm. in thickness on the flat, curved segments from the tubular areas of long bones may well present expanses of bone thicker than 1.4 cm. in vertical projection and cancellous specimens frequently can exceed the 1.4 cm. limit. The application of this technique to human beings, now in process, therefore, requires that the specimens be prepared, prior to packaging and irradiation, so that lying flat the vertical projection nowhere surpasses 1.4 cm. The other dimensions of the specimens are not limited in any way by the technique.

The absence of inflammation or foreign-body reaction to the irradiated grafts in these experiments parallels the findings of Meeker and Gross in their work on aortic segments. These authors have shown that the absence of significant deterioration in tissues by this sterilization procedure depends on maintaining them in a frozen state and using a dosage of 1.5 to 2.5 rep. Proctor and Goldblith [7] in their work with sterilization of foods recommend dosages of 1,000,000 to 1,500,000 rep, and this lower dosage may indeed be adequate, since the occasional example (3 in 125) of inadequate sterilization in Meeker and Gross' series [2] did not seem to be related to lower dosage levels. In our smaller series and in Proctor's no failures in sterilization were noted.

The failure of any of the grafts to produce bone is in accord with the findings of Reynolds and Oliver [3] and of Kruez and co-workers.[8] The reports by these authors of their investigation of thimerosal (Merthiolate) and freeze-drying sterilization contain histological material which corresponds rather closely to that described above. This is true not only for tissue reactions to bone sterilized by the two methods advocated by the authors, but also to sterile homogenous frozen bone. It seems as if all of these methods provide material similarly innocuous, to which the tissue reaction is at least not sufficiently dissimilar to favor one method over the others.

If we turn from consideration of tissue reaction to a comparison of the methods with respect to their theoretical reliability and their practical advantages or disadvantages, the following brief comment may be of interest. The thimerosal method offers the great advantage of simplicity of procedure and equipment, but, theoretically at least, it is a poor method to achieve bacteriological sterility. In fact, inactivation of bacteria by thimerosal may be reversible [9] and may occur only on surfaces. The freeze-dry method requires some special equipment, which now is becoming generally available; however, the method requires sterile processing throughout, since not only is it not bactericidal but it actually preserves bacteria.[10] The high-voltage cathode-ray sterilization method also presents the difficulty of using specialized equipment, but this is now available in a few centers (for food processing) and will soon be in general use. It offers the distinct advantages that it is the least harmful to tissues of all previous methods of sterilization and that it is an efficient bactericidal procedure.

SUMMARY

The application of high-energy cathode-ray irradiation to the sterilization of bone has been investigated. By this method homologous bone has been sterilized, and after storage in the frozen state implants were shown to be as successful in grafting procedures as untreated homologous bone. The method is a reliable means of sterilization of contaminated specimens without significant deterioration.

A parallel and concomitant study of this technique by members of the Tissue Bank of the U. S. Naval Hospital, Bethesda, Md. (G. W. Hyatt, T. C. Turner, and C. A. L. Bassett) was performed independently. The priority of this group in the adaptation of this method to bone grafts is freely acknowledged.

REFERENCES

1. Trump, J. G., and Van de Graaff, R. J.: Irradiation of Biological Materials by High Energy Roentgen Rays and Cathode Rays, J. Appl. Physics **19**:599, 1948.

2. Meeker, I. A., Jr., and Gross, R. E.: Sterilization of Frozen Arterial Grafts by High-Voltage Cathode-Ray Irradiation, Surgery **30**:19, 1951.

3. Reynolds, F. C., and Oliver, D. R.: Experimental Evaluation of Homogenous Bone Grafts, J. Bone & Joint Surg. **32-A**:283, 1950.

4. Grober, J., and Pauli, W. E.: Untersuchungen über die biologische Wirkung der Kathodenstrahlen, Deutsche med. Wchnschr. **45**:841, 1919.

5. Trump, J. G., and Van de Graaff, R. J.: A Compact Pressure Insulated Electrostatic X-Ray Generator, Physiol. Rev. **55**:1160, 1939.

6. Trump, J. G.; Wright, K. A., and Clarke, A. M.: Distribution of Ionization in Materials Irradiated by Two and Three Million-Volt Cathode Rays, J. Appl. Physics **21**:345, 1950.

7. Proctor, B. E., and Goldblith, S. A.: Electromagnetic Radiation Fundamentals and Their Applications in Food Technology, Advances Food Res. **3**:119, 1951.

8. Kreuz, F. P.; Hyatt, G. W.; Turner, T. C., and Bassett, A. L.: Preservation and Clinical Use of Freeze-Dried Bone, J. Bone & Joint Surg. **33-A**:863, 1951.

9. Dubos, R. J.: Bacterial and Mycotic Infections of Man, Philadelphia, J. B. Lippincott Company, 1952, p. 718.

10. Flosdorf, E. W., and Mudd, S.: Procedure and Apparatus for Preservation of Lyophile Form of Serum and Other Biological Substances, J. Immunol. **29**:389, 1935.

Surgery Illustrated

Techniques for Ureteropyeloplasty

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The surgeon will determine the exact plastic procedure at the operating table. Certain precautions will help insure good results:

1. Approach the renal pelvis through the lateral margin of Gerota's fascia rather than as far posteriorly as is customary. This provides a fatty pad behind and in front of the ureter to prevent fibrous adhesion to the posterior muscles.

2. Use nephrostomy (or pyelostomy) tubes and splints only when absolutely necessary, because they are irritating and introduce infection.

3. Use fine chromic sutures for reapproximation of pelvic and ureteral edges. Do not grasp edges with forceps.

4. Drain the area of repair accurately.

REFERENCES

1. Davis, D. M.: J. Urol. **66**:77-84, 1951.
2. Fenger, C.: J. A. M. A. **22**:335-343, 1894.
3. Gibson, T. E.: New England J. Med. **222**:910-917, 1940.
4. Priestley, J. T.: Surg. Gynec. & Obst. **68**:832-841, 1939.
5. Schwyzer, A.: S. Clin. North America **3**:1441-1448, 1923.
6. Foley, F. E. B.: J. Urol. **38**:643-672, 1937.
7. Ballenger, E. G., and McDonald, H. P.: J. Urol. **47**:203-208, 1942.
8. Küster, E.: Arch. klin. Chir. **44**:850-854, 1892.
9. Culp, O. F., and DeWeerd, J. H.: Proc. Staff Meet. Mayo Clin. **26**:483, 1951.

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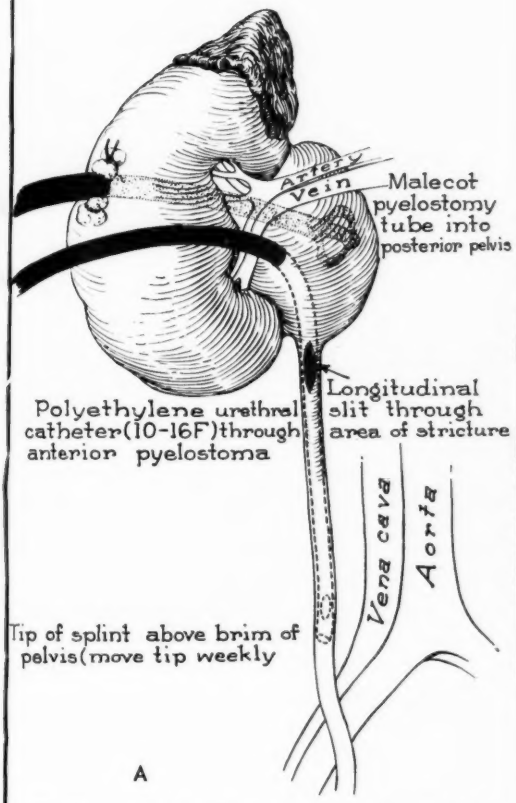

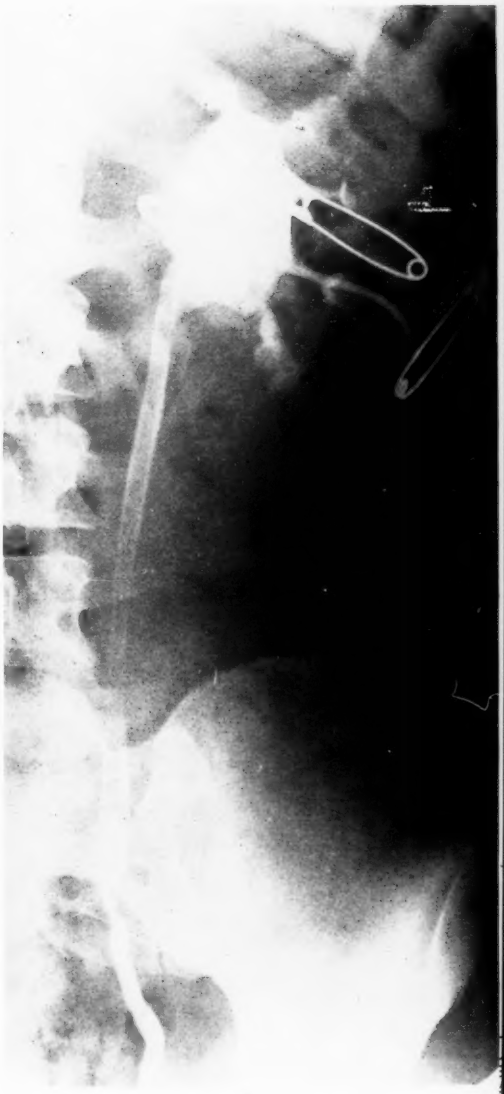

Fig. 1.—*A*, Intubated ureterotomy (Davis)[1]: Suitable for long strictures below the ureteropelvic juncture.

B, Nephrostogram showing splint and nephrostomy tube in place.

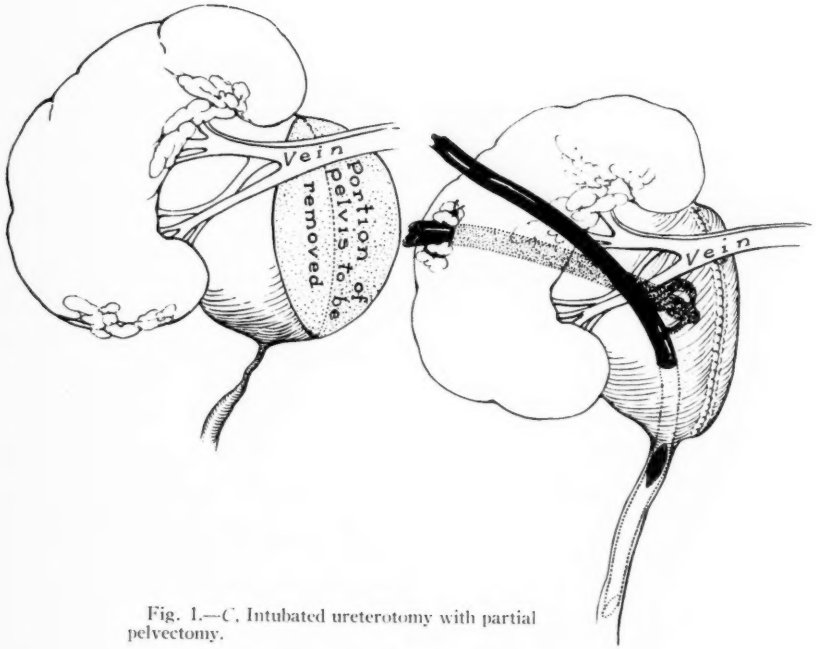

Fig. 1.—C, Intubated ureterotomy with partial pelvectomy.

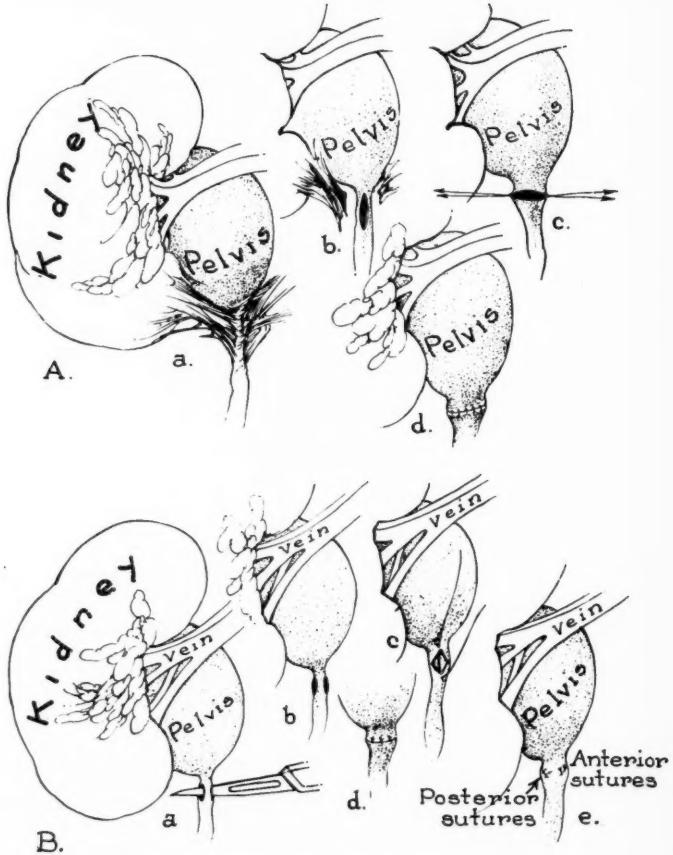

Fig. 2.—*A*, Pyeloureteroplasty using Heineke-Mikulicz principle (Fenger)[2]: A simple technique for short strictures.

B, Same with double incision (Gibson).[3]

A simple technique for short strictures.

B, Same with double incision (Gibson).[3]

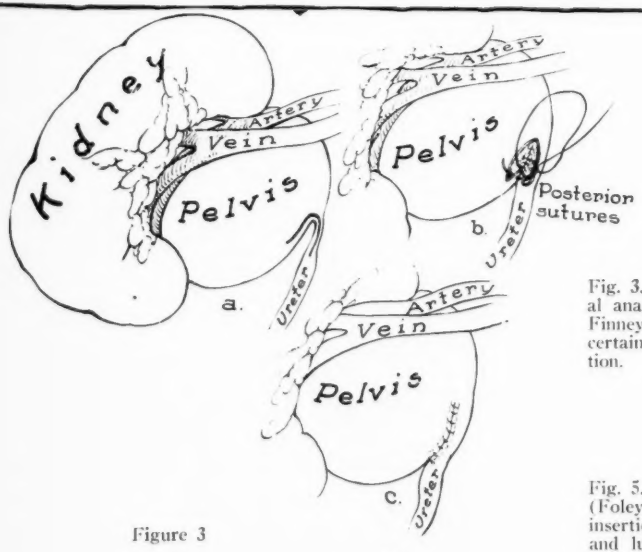

Figure 3

Fig. 3.—Pyeloplasty with lateral anastomosis (Priestley after Finney)[4]: An easy method for certain instances of high insertion.

Fig. 5. — Inverted Y-plasty (Foley)[6]: Excellent for high insertion; gives a better funnel and lumen than the Priestley-Finney method.

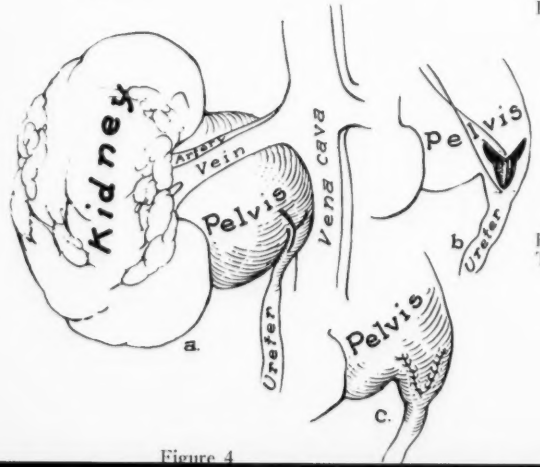

Figure 4

Fig. 4.—Y-plasty (Schwyzer)[5]: The classic method of repair.

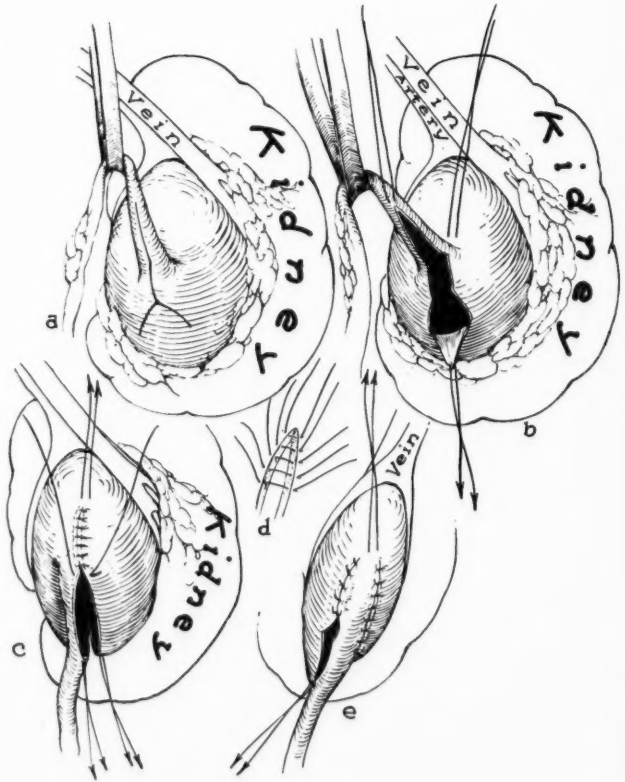

Figure 5

Fig. 6.—W-incision (Ballenger and McDonald).[7]

Fig. 7.— Reimplantation of ureter into pelvis: To be used with caution since the tip of the ureter may heal poorly.
A, Oblique reimplantation (Küster).[8]
B, With partial pelvectomy.

Fig. 8.—Flap pyeloplasty (Culp-Scardino)[9]: The newest technique; very good for moderately long strictures at and extending below the ureteropelvic juncture.